SEPTEMBER 6, 1952 PAGES 447 TO 494

THE LANCET

Offices: 7, ADAM STREET, ADELPHI, W.C.2
Telegrams: LANCET, RAND, LONDON **Telephone:** TEMPLE BAR 7228 and 7229

No. X OF VOL. II, 1952 LONDON, SATURDAY, SEPTEMBER 6, 1952 Pp. 96—Price 1s.
No. 6732 VOL. CCLXIII Founded 1823 PUBLISHED WEEKLY Registered as a Newspaper Annual Subscription: £2 2s.

for combined attack on Athlete's foot
and other fungal dermatoses

'MYCIL'

Contains chlorphenesin (p-chlorophenyl-e-glycerol ether)

Mycil ointment in collapsible metal tubes 2/6
Mycil dusting powder in sprinkler tins 2/6
Prices in Great Britain to the Medical Profession

THE BRITISH DRUG HOUSES LTD. (Medical Department) LONDON N.I
MYC/E/11

THE LIBRARY OF CONGRESS SERIAL RECORD SEP 22 1952

MAJOR ENDOCRINE DISORDERS
By S. LEONARD SIMPSON, M.A., M.D., F.R.C.P.
Consultant Endocrinologist, St. Mary's Hospital and Samaritan Hospital for Women; Endocrinologist, Princess Louise Children's Hospital.

"Thoroughly recommended to students, general practitioners, and consultants."—*British Medical Journal.*
Second Edition (1948) 574 pages 122 Illustrations 42s. net
Oxford University Press

THE LAW AND ETHICS OF DENTAL PRACTICE
By R. W. DURAND, M.R.C.S., L.R.C.P.
Formerly Secretary of the Medical Protection Society
and
D. MORGAN, L.D.S.(Leeds)
Formerly Deputy Dental Secretary of the British Dental Association
Foreword by Professor R. V. BRADLAW, M.D.S. Dunelm, F.D.S., M.R.C.S. Eng.
Professor of Oral Pathology, Durham University
Director, Newcastle-upon-Tyne Dental School

Expert guidance on the many problems which confront the dentist

Demy 8vo 98 + viii Price 7s. 6d. net, plus 4d. postage
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

Second Edition Now available
THE CARE OF TUBERCULOSIS IN THE HOME
By JAMES MAXWELL, M.D., F.R.C.P.
Physician, Royal Chest Hospital; Physician to the Ministry's Mass X-ray Unit; Consulting Physician, Royal National Sanatorium, Bournemouth; late Physician, St. Bartholomew's Hospital

Demy 8vo 114 + xii Illustrations 7s. 6d. net, plus 4d. postage
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

Second Edition
JOLL'S
DISEASES OF THE THYROID GLAND
By FRANCIS F. RUNDLE, M.D., F.R.C.S.
This is a complete revision of a work that has been a classic for twenty years.
530 pages 165 illustrations 84s
Wm. Heinemann · Medical Books · Ltd London

Second Edition Now available
SURGERY: A TEXTBOOK FOR STUDENTS
By CHARLES AUBREY PANNETT, B.Sc., M.D., F.R.C.S.
Professor of Surgery, University of London; Director of the Surgical Unit, St. Mary's Hospital, London; sometime member of the Court of Examiners, R.C.S. Eng., and Examiner to the Universities of London, Manchester, and Cardiff

769 + xiv Price 27s. 6d. net, plus 1s. postage
Extensively illustrated throughout text

Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

ENDOCRINE DISORDERS IN CHILDHOOD AND ADOLESCENCE
By H. S. LE MARQUAND, M.D.(Lond.), F.R.C.P.(Lond.)
Physician, Royal Berkshire Hospital
and F. H. W. TOZER, M.D.(Lond.), M.R.C.P.(Lond.)
Sometime Clinical Assistant, Royal Berkshire Hospital
Demy 8vo 298 + x pages Illustrated 15s., plus 5d. postage
Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

Fifth Edition Now available
PRINCIPLES OF MEDICAL STATISTICS
By A. BRADFORD HILL, D.Sc., Ph.D.
Demy 8vo 282 + x 10s. 6d. net, plus 6d. postage
With Twenty-five Exercises and Answers
The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2

BOOKS—New & Valuable

New (Ninth) Edition *Just Ready*
THE SCIENCE AND PRACTICE OF SURGERY
By W. H. C. ROMANIS, M.A., M.Ch., F.R.C.S., Senior Surgeon and Lecturer on Surgery, St. Thomas's Hospital; and PHILIP H. MITCHINER, *C.B., C.B.E.*, M.D., M.S., F.R.C.S., Hon. Surgeon to H.M. the Queen, and Consulting Surgeon, St. Thomas's Hospital
Vol. I. General Surgery. 20 Plates and 402 Text-figures. 32s.
Vol. II. Regional Surgery. 8 Plates and 326 Text-figures. 36s.

A TEXTBOOK OF GENERAL PHYSIOLOGY
By HUGH DAVSON, D.Sc. (Lond.). 288 Illustrations. 45s.

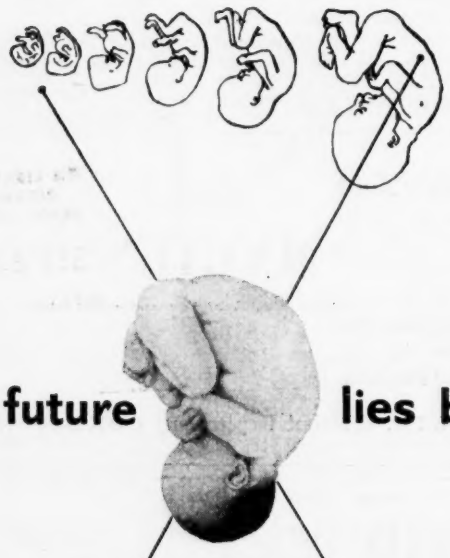
STARLING'S PRINCIPLES OF HUMAN PHYSIOLOGY
By Sir CHARLES LOVATT EVANS, D.Sc., F.R.S. *Eleventh Edition.* 709 Illustrations. 52s. 6d.

BIOCHEMISTRY FOR MEDICAL STUDENTS
By W. V. THORPE, M.A., Ph.D. *Fifth Edition.* 41 Illustrations. 22s. 6d.

SYNOPSIS OF REGIONAL ANATOMY
By T. B. JOHNSTON, *C.B.E.*, M.D. *Seventh Edition.* 20 Plates and 17 Text-figures. 22s. 6d.

ALL PRICES "NET"

J. & A. CHURCHILL LTD. 104 GLOUCESTER PLACE LONDON W.1



"GROWTH BEGINS WITH CONCEPTION . . ." The child at birth, his chances of survival and his early development are strongly influenced by the mother's diet . . . her own health and mental outlook are reflections of the food she eats . . .

But too often the food she eats is a reflection of long established habit. Normally, the average woman does not eat enough of the essential foods to meet both maternal and fetal requirements. To assure the daily intake of essential elements and to offset the wide variation in food composition even though the diet is adequate as described by the patient, DICALDIMIN provides protective amounts of minerals and vitamins.

his future lies behind him

Three capsules per day supply twice the recommended daily adult allowance of iron and nicotinamide for pregnant women, over three times that of riboflavine, six times that of aneurine hydrochloride, supplemental amounts of calcium and phosphorus and sufficient vitamin D in the form of viosterol to meet the entire daily requirement for this factor during pregnancy and lactation.

Dicaldimin is supplied in bottles of 100 *capsules.*

Dicaldimin

REGD. TRADE MARK

(*Calcium, Phosphorus, Iron and Vitamins, Abbott*)

Each Dicaldimin capsule represents:

Dicalcium Phosphate Anhydrous . . . 725 *mg.*
Ferrous Sulphate, B.P. . . . 50 *mg.*
Riboflavine, B.P. . . . 3 *mg.*
Aneurine Hydrochloride, B.P . . . . 3 *mg.*
Nicotinamide, B.P. . . . 12 *mg.*
Vitamin D (Calciferol), B.P. . . . 500 *i.u.*

Average dose
1 to 2 capsules three times daily with meals

Abbott

Literature and physicians sample available on request to:

ABBOTT LABORATORIES LTD
PERIVALE, GREENFORD, MIDDLESEX

SEPT. 6, 1952 PAGES 447 TO 494

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6732 LONDON: SATURDAY, SEPTEMBER 6, 1952 CCLXIII

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

The Dangers of Chronic Inactivity in the Aged
Mrs. A. V. HILL 447
Conversion of Tissue Polysaccharides to Auto-antigens by Group-A Beta-hæmolytic Streptococci
L. E. GLYNN, M.R.C.P.
E. J. HOLBOROW, M.B. 449
Deforming Factors in the Early Stage of Poliomyelitis
G. P. MITCHELL, F.R.C.S.E. ... 451
Salt-losing Nephritis
C. L. JOINER, M.R.C.P.
M. G. THORNE, M.R.C.P. 454
The Condition of the Kidneys in Salt-losing Nephritis
J. B. ENTICKNAP, M.D. 458
Retardation of Growth Associated with Hirschsprung's Disease
Prof. F. A. R. STAMMERS, F.R.C.S.
A. J. H. RAINS, F.R.C.S. 461
Treatment of the Adrenogenital Syndrome with Cortisone
DOUGLAS HUBBLE, M.R.C.P. ... 464
Thiopentone followed by Nitrous Oxide and Oxygen for Anæsthetising Outpatients
E. H. FRANKS, M.B. 466
Tetraethyl Lead Poisoning
GEOFFREY WALKER, M.B.
P. R. BOYD, M.B. 467

PUBLIC HEALTH

The Need for an Occupational Hygiene Service
P. H. NASH, M.D. 478
Poliomyelitis 479
International Certificates of Vaccination 479

NEW INVENTIONS

Modification of Bonney-Reverdin Needle-holder
ROBERT PERCIVAL, F.R.C.S. 469

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents ... 483

LEADING ARTICLES

WHAT OF GENERAL PRACTICE ? .. 471
ISONIAZID TRIALS 471
ATROPINE ALKALOIDS 472

ANNOTATIONS

Diurnal Excretory Rhythm 474
Advances of Science 474
Valvulotomy versus Shunt 474
Getting into Step 475
Isotopes in Britain 475
Streptococci and Rheumatism ... 476
Sex-hormone Metabolism in Liver Disease 477
Death after Inoculation 477

POINTS OF VIEW

Cure of Tobacco-smoking
LENNOX JOHNSTON, M.B. 480

MEDICINE AND THE LAW

Murder and Abnormality 479

LETTERS TO THE EDITOR

The Prospect of General Practice (Dr. Andrew Smith; Dr. F. Charlotte Naish; Dr. W. P. Jenson; Dr. L. M. Green; Dr. Duncan Milne; Dr. G. L. Davies; Mr. J. D. Wigdahl; Dr. S. Lipetz; Dr. W. A. Ball) 484
Lead Paint: a Hazard to Children (Sir Allen Daley, F.R.C.P.; Dr. M. B. Morris) ... 486
Action of Antibiotics (Dr. Derrick Rowley) 487
Attendance at Boxing Contests (Dr. J. L. Blonstein) 487
Blood-pressure Estimations in Children (Dr. G. E. Breen) 487
Carob Flour in Functional Vomiting of Infants (Dr. Theodore James) 487
Nurses in the Making (Dr. George McCoull) 488
Incision for Appendicectomy (Mr. John McDonald, F.R.C.S.E.) ... 488
Hypoglycæmia in Road Users (Dr. R. D. Lawrence) 489
Fluorine Intake in Britain (Dr. Dagmar Wilson) 489
Bone Regeneration (Prof. G. M. Wyburn, F.R.F.P.S.) 489
Feeding Disorders in Infants (Miss Madeleine Pottenger) 490
Books on Hospitals (Dr. William Hartston) 490
Treatment of Pulmonary Tuberculosis (Dr. J. P. Anderson; Mr. L. J. Temple, F.R.C.S.) 490
Megaloblastic Anæmia of Pregnancy (Dr. H. O. Nieweg) 491
Achalasia *v.* Cardiospasm (Dr. R. E. Smith) 491
Chlorophyll as Deodorant (Mr. N. W. Pirie, F.R.S.; Mr. L. Deadman) 492
Functional Disorders of the Small Intestine (Dr. A. J. Glazebrook) 492

REVIEWS OF BOOKS

William Smellie 469
An Explaining and Pronouncing Dictionary of Scientific and Technical Words 470
The Art of Marriage 470
Medicinal Chemistry 470
Surgical Gynecology 470

OBITUARY

John Geoffrey Cutts 492

NOTES AND NEWS

Capital Expenditure on Hospitals 493
Senior Registrars in the North-west Metropolitan Region 493
Royal College of Obstetricians and Gynæcologists 493
Institute of Laryngology and Otology 493
Royal Institute of Public Health and Hygiene 493
Postgraduate Courses for General Practitioners at Cambridge ... 493
British Postgraduate Medical Federation 493
King's College Hospital, London 493
Appointments 494
Births, Marriages, and Deaths .. 492

APPLIED PHYSIOLOGY

by SAMSON WRIGHT, *M.D., F.R.C.P.*
John Astor Professor of Physiology in the University of London, Middlesex Hospital Medical School
With the collaboration of
MONTAGUE MAIZELS, *M.D., F.R.C.P.*
Professor of Clinical Pathology in the University of London, University College Hospital Medical School
and
JOHN B. JEPSON, *M.A., B.Sc., D.Phil., A.R.I.C.*
Senior Lecturer in Biochemistry, Courtauld Institute of Biochemistry, Middlesex Hospital Medical School

NINTH EDITION 1206 *pages* 688 *illustrations* 4 *coloured plates* 50s. *net*

OXFORD UNIVERSITY PRESS

The Complex Nature of Deficiency Conditions

Nutritional deficiencies in general, and vitamin deficiencies in particular, can rarely be attributed to the absence of a single factor. Treatment with a single synthetic factor alone is therefore not usually recommended.

In the case of the B_2 vitamins, which appear to act synergistically, it is especially important to administer a source of the whole group, either alone or in addition to a single factor. As a source of the vitamin B_2 complex, Marmite yeast extract has been found exceptionally useful, because it is easily administered and supplies these vitamins in the naturally occurring state.

MARMITE
yeast extract

contains
Riboflavin (vitamin B_2) 1·5 mg. per oz.
Niacin (nicotinic acid) 16·5 mg. per oz.
Obtainable from chemists and grocers
Special terms for packs for hospitals, welfare centres and schools
Literature on request
The Marmite Food Extract Co., Ltd., 35, Seething Lane, London, E.C.3

6209

BRITISH EMPIRE CANCER CAMPAIGN

A SURVEY OF CANCER IN LONDON

REPORT OF THE CLINICAL CANCER RESEARCH COMMITTEE

By
W. L. HARNETT, C.I.E., M.D., F.R.C.S.,
Medical Secretary to the Committee.

With a *Foreword* by the
Rt. Hon. Lord HORDER, G.C.V.O., M.D., F.R.C.P.

And an *Introduction* by
Sir HENEAGE OGILVIE, K.B.E., D.M., M.Ch., F.R.C.S.

Pp. vi + 834, with 22 figures in the Text.

Price: bound in paper covers **45s.**, *in cloth* **50s.**
Packing and postage: Inland 2*s.* 9*d.*, *Canada* 7*s.*, *U.S.A.* 7*s.* 6*d.*

BRITISH EMPIRE CANCER CAMPAIGN
11, Grosvenor Crescent, London, S.W.1

There is only ONE

XYLOCAINE*

THE NEW LOCAL ANAESTHETIC

—Product of Original Research

Now available in Packings and Preparations suitable for all Local Anaesthetic Techniques

DUNCAN, FLOCKHART & CO., LTD.
SPECIALISTS IN ANAESTHETICS
EDINBURGH LONDON

*Regd. Trade Mark

HENRY KIMPTON'S PUBLICATIONS

New Edition — Ready this Month

THE TREATMENT OF DIABETES MELLITUS

By **ELLIOTT P. JOSLIN**, A.M., M.D.; **HOWARD F. ROOT**, M.D.; **PRISCILLA WHITE**, M.D.; and **ALEXANDER MARBLE**, A.M., M.D.

NINTH EDITION, REVISED

Royal Octavo | 771 Pages | Illustrated | Cloth | Price **90s.** net

New Book — Ready this Month

THE KNEE AND RELATED STRUCTURES

Injuries—Deformities—Diseases—Disabilities

By **PHILIP LEWIN**, M.D., F.A.C.S., F.I.C.S.

Royal Octavo | 914 Pages | 333 Illustrations and 2 Coloured Plates | Cloth | Price **£6** net

New Book — Ready this Month

NORMAL BLOOD PRESSURE AND HYPERTENSION

New Definitions

By **ARTHUR M. MASTER**, M.D.; **CHARLES I. GARFIELD**, M.D.; and **MAX B. WALTERS**, M.D.

Royal Octavo | 144 Pages | 36 Illustrations | Cloth | Price **30s.** net

New Edition — Ready Shortly

THE AUTONOMIC NERVOUS SYSTEM

Anatomy, Physiology, and Surgical Application

By **JAMES C. WHITE**, M.D.; **REGINALD H. SMITHWICK**, M.D.; and **FIORINDO A. SIMEONE**, M.D.

THIRD EDITION, REVISED

Royal Octavo | 569 Pages | Illustrated | Cloth | Price **90s.** net

New Book — Now Ready

GASTROINTESTINAL X-RAY DIAGNOSIS

By **MAX RITVO**, M.D., and **I. A. SHAUFFER**, M.D.

Large Octavo | 838 Pages | 470 Illustrations, including 2 in Colour | Cloth | Price **£7 10s.** net

New Book — Now Ready

PRINCIPLES AND PRACTICE OF ANESTHESIOLOGY

By **VINCENT J. COLLINS**, M.D.

Royal Octavo | 528 Pages | 99 Illustrations | Cloth | Price **75s.** net

25 Bloomsbury Way **HENRY KIMPTON** **London, W.C.1**

Medical Book Department of Hirschfeld Brothers Ltd.

CLANOID

L.I.R.B.M.

COMBINING

- ***Liver Extract***
- ***Ferri et Ammon Cit***
- ***Red Bone Marrow***
- ***Liquid Extract of Malt***

An ideal nutritional adjuvant and hæmatinic tonic for infants, children and adults. 2 oz. bottles, with dropper, 4-8-16 oz.

Write for literature and samples to :—

Telephone : CLERKENWELL 9011

Telegrams : "ARMOSATA-PHONE" London

THE ARMOUR LABORATORIES

(ARMOUR & COMPANY LTD)

LINDSEY STREET, LONDON, E.C.1

If aspirin were freely soluble
and bland–

If calcium aspirin were stable
and palatable–

That would be 'Solprin'

SOLPRIN
REGD.

Provides stable, soluble, palatable calcium aspirin

Clinical sample and literature supplied on application. Solprin is not advertised to the public and is available only on prescription. (U.K. and Northern Ireland only). Dispensing pack, price 8/- (Purchase Tax Free) contains 300 tablets in foil.

RECKITT & COLMAN LTD., HULL AND LONDON. (PHARMACEUTICAL DEPT., HULL)

ELIXIR CEREVON

C.
FERROUS GLUCONATE

**Anæmias of Pregnancy*

PROVIDES ORGANIC IRON

* *(B.M.J., 23.2.52, p. 407.)*

"... It was found that 33% of the patients in group A and 40.2% in group C found it difficult or impossible to tolerate ferrous sulphate tablets, and it can be assumed that between 30 and 40% of all antenatal patients will not, in fact, take these tablets if they are routinely prescribed in the antenatal department."

The need for a more suitable form of iron for the treatment of iron deficiency anæmias of pregnancy is evident.

Clinical trials have shown that for tolerance, absorption and utilisation the organic iron of FERROUS GLUCONATE as presented in Elixir Cerevon is more acceptable to the gastric mucosa and hæmapoietic system.

Elixir Cerevon also provides adequate doses of the important factor of the Vitamin B complex and the inclusion of 15% blackcurrant juice provides approximately 5.0 mgm. Vitamin C per teaspoonful and makes the preparation highly palatable.

FORMULA: Each teaspoonful contains; Ferrous Gluconate 0.3 gm.; Aneurine Hydrochloride 1 mgm.; Riboflavin 1 mgm.; Nicotinamide 10 mgm. With trace elements of Copper and Manganese.

PACKS: Bottles of 4 fl. ozs. and 80 fl. ozs.

Prescribe ELIXIR CEREVON by name

Literature available on request from the Medical Department

CALMIC LIMITED · MANUFACTURING CHEMISTS · CREWE · Tel. 3251-5

B_{12} enters general practice

Among the many factors contributing to sound nutrition, vitamin B_{12} is taking a recognised place. Its marked tonic effect when given by injection has been widely recognised; and, more recently, the introduction of CYTACON has enabled doctors to give the vitamin *by mouth* for purely nutritional purposes.

In appropriate cases, the effects of CYTACON have been most promising; they include increase in appetite, improvement in general well-being during convalescence, and accelerated weight gain in underweight children. And, because it seems that oral B_{12} has especial value in the treatment of the younger patient, CYTACON is issued not only in tablet form but also as a sweet, pleasantly flavoured liquid—for teaspoonful dosage.

CYTACON
Trade mark

Tablets: 10 micrograms; bottles of 50 and 500

Liquid: 25 micrograms per fluid drachm; bottles of 6 fl. ozs.

GLAXO LABORATORIES LIMITED, GREENFORD, MIDDLESEX BYRon 3434

STRAINS & SPRAINS

A new approach to Vaso-Dilatation

New powerful penetrative agent ensures subcutaneous penetration of histamine

IT has long been recognised that histamine, in dilating the capillaries, acts as a pain-reliever. In 'Algipan' the difficulty hitherto experienced in applying the drug to the subcutaneous layers without injection has now been overcome. The potent penetrative agent methyl nicotinate enables surface applications of histamine to reach the deeper tissues, where it promotes an increased flow of blood and relieves pain. A comforting rubefacient action is exerted by the glycol salicylate and capsicin.

The penetrative, warming and pain-relieving properties of 'Algipan' bring rapid relief. 'Algipan' is a pleasant non-greasy, water-soluble cream, and only a very gentle rubbing is needed.

WINGS DAY SEPT 20th
Give for those who Gave

'Algipan'
*Trade Mark.

JOHN WYETH & BROTHER, LTD., CLIFTON HOUSE, EUSTON ROAD, LONDON, N.W.1.
*The Trade Mark is the property of Laboratoires Midy, Paris.

AN ANALYSIS OF CLINICAL REPORTS ON

Preceptin REGD.

VAGINAL GEL

A NEW CONTRACEPTIVE GEL

CLINICAL REPORTS

—from abstracts of papers read before the Biology Section, New York Academy of Sciences, New York City, Oct. 19-20 1951.

1. Clinical Experience with a New Gel-Alone Method of Contraception

"... the pregnancy rate in this study was 4.1 for the entire group (467 patients). There were 5 pregnancies in the series of women using the Gel ... an effectiveness of 97.9 per cent."*

2. A Method of Contraception Without Diaphragm

"Aesthetic acceptability and effectiveness in preventing conception were ascertained through a questionnaire and by study of the charts. ... During the two year study of this contraceptive Gel, conception was effectively controlled in 98.2 per cent of the 704 patients."*

CLINICAL RESULTS

—from a survey made in 51 urban and rural areas.

In a controlled study of 5599 women who used PRECEPTIN vaginal gel under the direction of their physicians 3270 case histories submitted and examined showed only 25 pregnancies—99.2 per cent received complete protection.

The average patient was 26.9 years of age and had had 4.3 pregnancies prior to this study. PRECEPTIN vaginal gel's combination of simplicity and dependability makes for extremely high contraceptive effectiveness.

Preceptin is a registered trade mark and is protected by world patents.

PRECEPTIN vaginal gel—a major advance in conception control developed by Ortho Research Laboratories.

COMPOSITION: PRECEPTIN vaginal gel contains the active spermicidal agents p-Diisobutylphenoxypolyethoxyethanol and ricinoleic acid in a synthetic base buffered at pH 4.5.

BIBLIOGRAPHY

*International Record of Medicine and General Practice Clinics *(1)* 164:674 (Nov.) 1951. *(2)* 164:675 (Nov.) 1951.

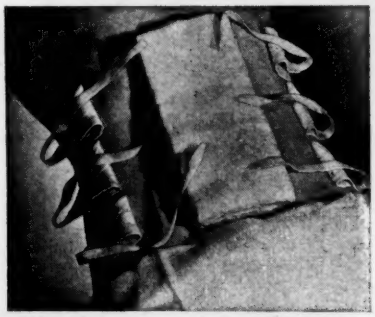
Ortho Pharmaceutical Limited

HIGH WYCOMBE · BUCKINGHAMSHIRE · ENGLAND

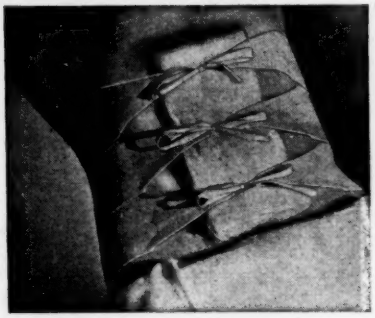
Associated Companies: Raritan, U.S.A.; Toronto, Canada; Sydney, Australia.

Elastoplast as a many-tailed bandage

When frequent dressings are necessary, the following method of applying Elastoplast may be used as a substitute for an abdominal many-tailed bandage.



Above: Fig. 1 *Below: Fig. 2*



Prescribe Elastoplast Bandages by name on form E.C.10

SIX PIECES, each about 12 inches in length, are prepared from a 3 inch wide Elastoplast bandage. Tapes are attached and the completed pieces applied to the body from each side (Fig. 1). The tapes are tied over the dressing covering the wound (Fig. 2). The bandage may be applied by one person without disturbing the patient. It is easily made, provides adequate support and will remain firmly in position.

The above method is comfortable in use as the patient does not have to wear perineal stirrups to keep the bandage in place or to lie on a bandage which may become 'rucked-up' — disadvantages associated with the flannelette type of many-tailed bandage.

Elastoplast
TRADE MARK

is made by T. J. Smith & Nephew Ltd., Hull. Outside the British Commonwealth, Elastoplast is known as Tensoplast

For promoting *Natural Restful Sleep*

INSOMNIA frequently presents a problem which cannot be effectively and safely solved by recourse to the use of hypnotics.

In these circumstances 'Ovaltine' will often induce natural, restful sleep. This effect is especially valuable when sleeplessness results from dyspepsia or neurasthenia. Because 'Ovaltine' is so readily assimilated and metabolized, its use encourages sleep which remains undisturbed overnight.

'Ovaltine', prepared from highest quality natural foods, provides important "proximate principles" and vitamins; delightful to taste, it is equally appreciated by children and adults.

Ovaltine

Vitamin Standardization per oz:—
Vitamin B_1, 0·3 mg.; Vitamin D, 350 i.u.; Niacin, 2 mg.

A. WANDER LIMITED, 42 Upper Grosvenor Street, Grosvenor Square, London W.1.

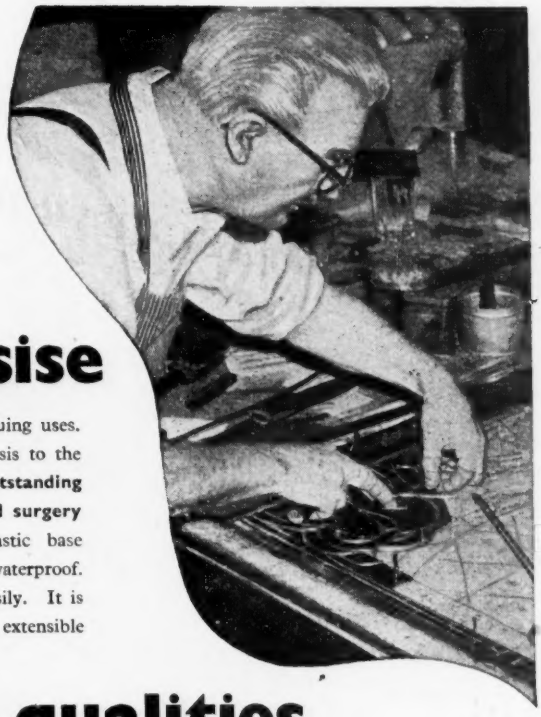
M.335

S. 31

...ANOTHER UNUSUAL USE FOR **'Sleek'**

plastic zinc oxide adhesive strapping

Gleaming, beautiful pieces of stained glass can cut and scratch the nimblest of fingers, and the artist-craftsman, no less than the glazier, has need of protection. Finger-tips covered with 'Sleek' are no less deft, and how confidently the work proceeds in skilled hands so surely protected.



to emphasise

Yes, 'Sleek' does get put to some intriguing uses. These unusual jobs lend dramatic emphasis to the unique qualities which make 'Sleek' of **outstanding value for everyday use in hospital and surgery practice.** Above all, because the plastic base material is impervious to liquids, it is waterproof. 'Sleek' is washable, yet does not soil easily. It is smooth and thin yet very strong. It is extensible and pliable. It does not 'catch' or fray.

8 valuable qualities

WATERPROOF · GREASEPROOF · WASHABLE · SMOOTH

THIN · STRONG · PLIABLE · NON-FRAYING

'Sleek' TRADE MARK **plastic zinc oxide adhesive strapping**

In 2½ yd. rolls, 1" wide. In 5 yd. rolls, 1", 2", 3" and 4" wide. FREE SAMPLE sent on request.

Also

'HANDYPLAST' elastic wound dressing. With an AIR-STRIP to promote quicker healing. Strips, 1½" and 2½" wide and packs of assorted dressings.

'LEUKOPLAST' zinc oxide adhesive plaster. Laboratory controlled to ensure constant and uniform quality of the cotton cloth and adhesive strength. In 5 yd. and 10 yd. rolls, ½", 1", 2" and 3" wide.

HERTS PHARMACEUTICALS LTD., WELWYN GARDEN CITY, ENGLAND

Sympatol

A CARDIOVASCULAR DRUG

Brand p-Methylaminoethanolphenol tartrate

PACKING AND SIZES:

Sympatol liquid 10%
Bottles of 20 cc.
Bottles of 100 cc.
Sympatol ampoules (0,06 g) for injection
Boxes of 6 ampoules
Hospital Pack
of 30 ampoules

For the treatment of collapse

For the treatment of constitutional hypotension

For the management of hypotensive conditions in infectious and chronic illnesses

LEWIS LABORATORIES · LTD · LEEDS

Hyperacidity:

WHY

ALIMEX?

1 *Prompt and sustained relief from pain and discomfort*

2 *Maximal acid-binding capacity*

3 *No risk of alkalosis*

4 *Minimal interference with normal digestion*

5 *Palatable and acceptable for prolonged administration*

6 *Bland and non-constipating*

Alimex is a pleasantly flavoured preparation of aluminum hydroxide with magnesium hydroxide. It corrects gastric hyperacidity, relieves gastro-intestinal irritation and is, therefore, a valuable adjunct in the medicinal treatment of peptic ulcer.

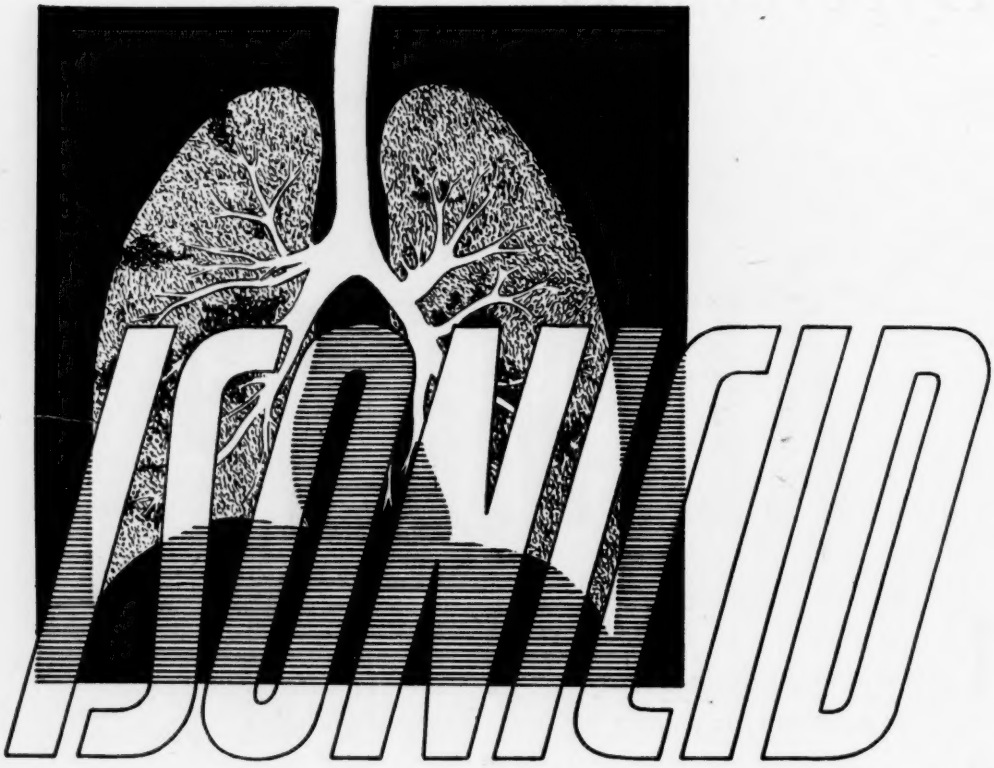
Bottles of 8 fl. oz. and in bulk for dispensing purposes.

Literature and further information on request from the Medical Department
BOOTS PURE DRUG COMPANY LIMITED NOTTINGHAM ENGLAND

Boots

8143

11



iso-nicotinic acid hydrazide

brings **NEW STRENGTH**
NEW HOPE
NEW LIFE
for tuberculotics

ISONICID is supplied as tablets of 50 mg. each
Bottles of 100 and 1000

Clinical samples and literature gladly sent on request

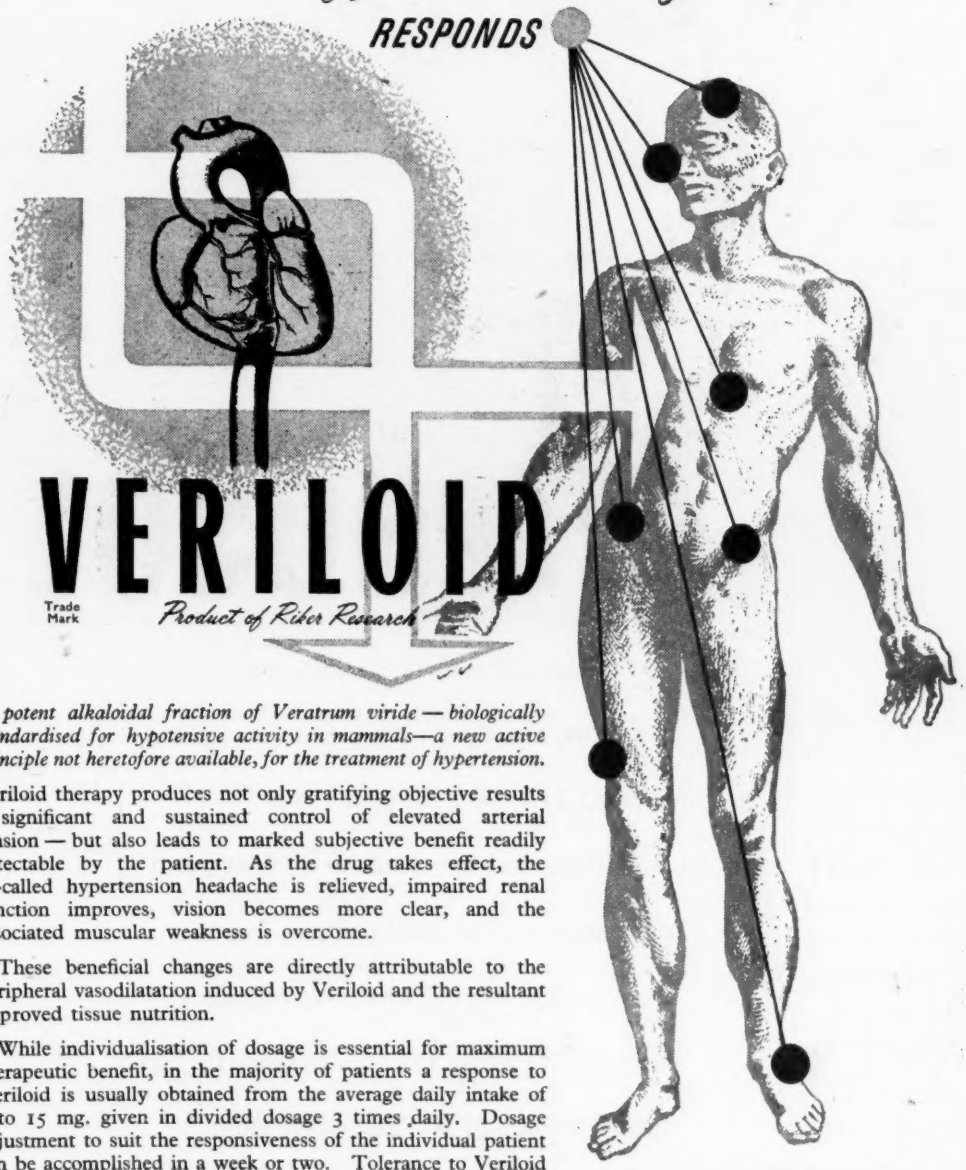
by

MEDIMPEX

Hungarian Trading Company for Pharmaceutical Products
BUDAPEST 62, P.O.B. 326 HUNGARY

The Hypertension Syndrome

RESPONDS



VERILOID

Trade Mark

Product of Riker Research

A potent alkaloidal fraction of Veratrum viride — biologically standardised for hypotensive activity in mammals—a new active principle not heretofore available, for the treatment of hypertension.

Veriloid therapy produces not only gratifying objective results — significant and sustained control of elevated arterial tension — but also leads to marked subjective benefit readily detectable by the patient. As the drug takes effect, the so-called hypertension headache is relieved, impaired renal function improves, vision becomes more clear, and the associated muscular weakness is overcome.

These beneficial changes are directly attributable to the peripheral vasodilatation induced by Veriloid and the resultant improved tissue nutrition.

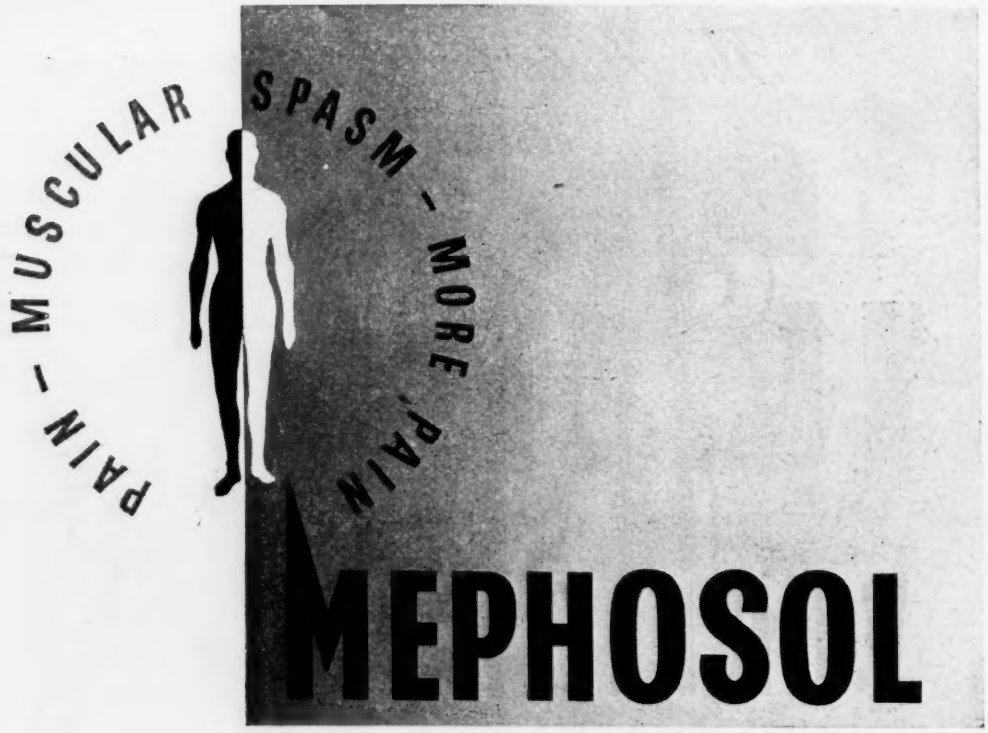
While individualisation of dosage is essential for maximum therapeutic benefit, in the majority of patients a response to Veriloid is usually obtained from the average daily intake of 9 to 15 mg. given in divided dosage 3 times daily. Dosage adjustment to suit the responsiveness of the individual patient can be accomplished in a week or two. Tolerance to Veriloid is not likely to develop, and treatment can be continued indefinitely without deleterious effect.

Veriloid is available on prescription only through all pharmacies in 1 mg. and 2 mg. tablets in bottles of 100 and 500. ‡ Literature available on request.

RIKER LABORATORIES LTD.,
29, KIRKEWHITE STREET, NOTTINGHAM.

VERILOID-VP AND VERILOID INTRAVENOUS

Veriloid is also available as Veriloid-VP, containing Veriloid 2 mg. and Phenobarbitone B.P. 15 mg. for administration to patients who find it difficult to tolerate Veriloid alone.
For injection in cases of hypertensive crises, it may be obtained in ampoules containing Veriloid 0.4 mg. per c.c. in 0.25% acetic acid, under the style of Veriloid Intravenous Solution.

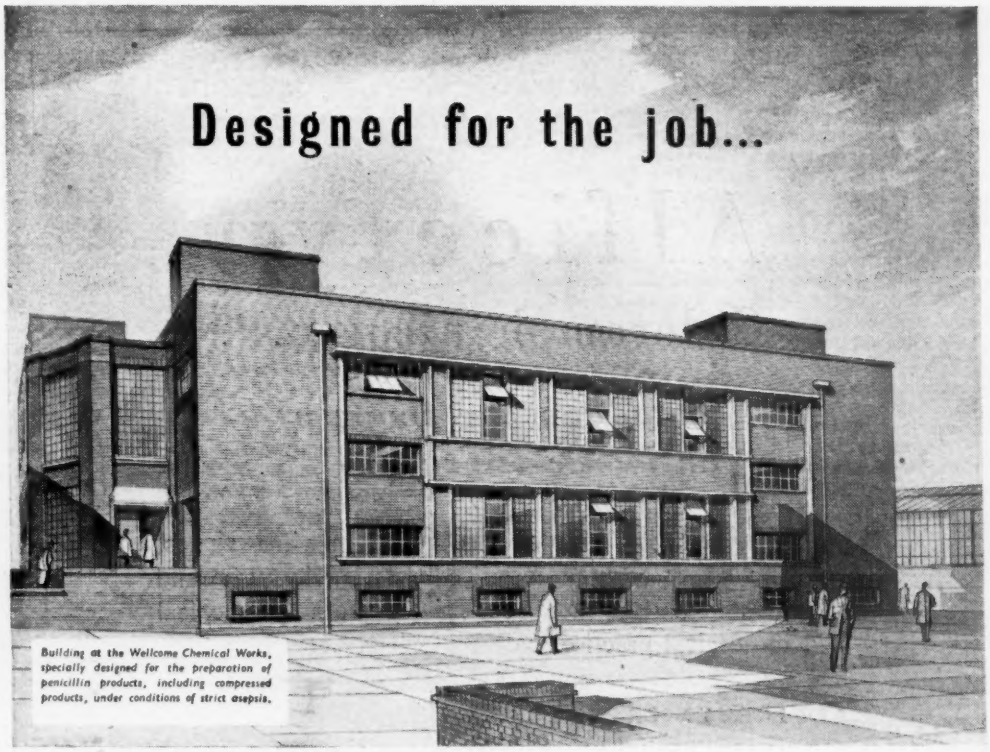


In rheumatic disorders the commonest symptom, and the most trying to the patient, is pain. Following the pain comes muscle spasm, which leads to disability, loss of function — then more pain, more spasm. MEPHOSOL (containing mephenesin) breaks this vicious circle by the direct abolition of skeletal muscle pain. It is analgesic and antispasmodic.

CROOKES
MEPHOSOL
TRADE MARK

THE CROOKES LABORATORIES LIMITED · PARK ROYAL · LONDON · N.W.10

Designed for the job...



Building at the Wellcome Chemical Works, specially designed for the preparation of penicillin products, including compressed products, under conditions of strict asepsis.

The B.W. & Co. range of penicillin preparations, including compressed products, is designed to simplify administration, to save valuable professional time and to produce the greatest therapeutic effect at the site of infection. For example, effective blood concentrations without recourse to continuous injections may be obtained with 'Tabloid' brand Penicillin Oral or by using one of the depot injections—'Wellcome' brand Oily Injection of Procaine Benzylpenicillin, or 'Wellcome' brand Oily Injection of Penicillin. In eye conditions, 'Tabloid' brand Ophthalmic Benzylpenicillin, placed in the conjunctival sac, brings the antibiotic into immediate contact with the affected part. Oral infections are best treated by 'Tabloid' brand Penicillin Lozenge, while for preparation of small quantities of solutions for eye drops or cream, 'Tabloid' brand Hypodermic Benzylpenicillin has everything to recommend it.

B.W.& CO. PENICILLIN PRODUCTS

BURROUGHS WELLCOME & CO. (The Wellcome Foundation Ltd.) LONDON

Alficetyn BRAND

Chloramphenicol B.P.

broadens the scope of antibiotic therapy

Chloramphenicol has proved effective in vitro against a vast number of gram-negative bacteria, rickettsiæ and viruses and is indicated extensively both in medical and in surgical practice.

ALFICETYN CAPSULES

For oral administration. Available in bottles of 12 capsules each containing 0·25 gramme Chloramphenicol B.P.

ALFICETYN SUPPOSITORIES

Containing 0·125 gramme and 0·25 gramme Chloramphenicol B.P., in boxes of 5.

ALFICETYN EAR DROPS

Containing a 10% solution of Chloramphenicol B.P., in vials of 5 c.c. with a suitable dropper applicator.

ALFICETYN EYE OINTMENT

Containing 1% Chloramphenicol B.P., in collapsible tubes of 60 grains

Literature on the above A & H products on request.

ALLEN & HANBURYS LTD · LONDON · E·2

TELEPHONE: BISHOPSGATE 3201 (20 LINES). TELEGRAMS: "GREENBURYS, BETH, LONDON"

THE DANGERS OF CHRONIC INACTIVITY IN THE AGED*

MARGARET HILL

BETWEEN 1871 and 1950 the number of old men and women has increased from $1^1/_4$ million to $5^1/_2$ million. It is estimated that in another 20 years there will be nearly 10 million people of pensionable age. Although in 1931 there were about four times as many young women as old, there are now only a little over twice as many. The burden on the social services and on the wage-earners will then be proportionately even heavier than it is now.

It is easy to think of old people as infirm old people, as these are so much more in evidence than the rest. Actually the number in hospitals and institutions is only between 3% and 5% of the total number of the old, although many others are desperately in need of care of some sort though not necessarily in institutions. There is a great deal of untreated disease in old people, and it must always be remembered that the process of growing old, apart from disease, produces biological changes, none of which are to the good. The problem which must be faced, unless an intolerable burden is to be borne by the younger members of the community, is how to prevent unnecessary illness in the middle-aged and elderly.

IMPORTANCE OF EARLY TREATMENT

Modern medicine is lengthening life in all countries, yet the best methods of dealing with chronic ill health in the old have not received sufficient attention. Much could be done at earlier stages and this is the all-important matter at the present time. The first preventive is to provide suitable living conditions so that old people may live independently and manage their own affairs for a longer period. From the point of view of activity which is essential to well-being there is nothing to excel the work involved in doing their own household chores, and the necessity for getting out regularly in all weathers to do their shopping. No contrived activities are so valuable or so health-giving as the necessary acts involved in living alone and independently. The emphasis must be on keeping the middle-aged young as it is difficult to rejuvenate the old; but even for these latter fresh air and exercise, no lying in bed unless absolutely necessary, good food, the absence of apprehension for the future, and the companionship of others of their own generation can do much to alleviate their disabilities.

I have had considerable opportunity of observing all this from a housing trust which has now been in existence for over twenty years. During this period some 320 people, most of them old, have been accommodated, and of the 48 who have died only 2 did so in hospital. All the rest stayed in their homes to the end. They were provided with visiting nurses and home helps where necessary. How much more economical for the community, and how much happier for the old people, if simple comfort and security of tenure in suitable surroundings enables them to live at home until the end.

HOUSING FOR THE OLD

While the more vigorous old undoubtedly like a little extra space and the privacy of a small flat, a single room with every convenience is better later on. I regret that in planning for the future, authorities and organisations are still preparing to provide perfection for the few and nothing for the rest. They could comparatively easily provide single rooms, with common bathroom and water closet for tenants on the same floor, either by building or by the conversion of larger dwelling houses, for a fraction of the cost of erecting blocks of self-contained flats. It is not even certain that the perfect flat is always appreciated or preferred. As a general rule it is far better for people of not more than two generations to live together, and undoubtedly it is happier for the older folk to live independently, and so remain active in the course of looking after themselves, rather than to try to adapt their lives to those of younger people or to become entirely dependent upon them for their care. Although there are happy family groups, especially in the country, on the whole old people prefer their own little home wherever possible. When the security of their own home is absent it may make them unwilling to go to hospital for essential treatment, fearing that they may lose both home and independence while away. Fear that old people may be left on their hands may prevent hospitals from taking them for treatment in the early stages when chronic illness might be prevented. Despite the shortage of beds many old people have to be taken to hospital or institution for purely domestic reasons rather than because of ill health. To keep sick old people from deteriorating into chronic invalids because of the lack of mental and physical stimulation of any kind is of the greatest importance. It is even more weakening for the elderly to remain in bed than for younger patients, owing to their lack of resilience.

SUITABLE FORMS OF ACTIVITY

From birth onwards exercise is necessary to health, and this still holds good in old age. It is far too easy, often with the encouragement of relatives, for an old person to get into the habit of spending much time in bed and the rest of the day sitting by the fire instead of making the effort to put on outdoor clothes and get going. I have rarely seen harm come from the daily walk, even for those in frail health, if they can manage it, and it is undoubtedly stimulating both to mind and body. Going up and down stairs in moderation is good exercise and is especially beneficial in keeping joints flexible. With children it is often easier to do the work than to allow them to help, as they would like to do, and the same thing applies to the old whether in their relatives' homes or in residential establishments: but it is undesirable.

Over-anxiety for the old may be as harmful as neglect. This is often so with old people living with their families. In the name of kindness they are gradually prevented from any activity or independence and this finally wears them down. I have several times met interesting examples of this.

Mrs. J was married to a man considerably younger than herself who waited on her hand and foot. She allowed him to do more and more—the cooking, the shopping, and the housework—while she became less and less active and simply sat about or lay in bed smoking cigarettes; she even reached the stage of incontinence through laziness. Then one day her husband had a seizure and was removed to hospital. Mrs. J was cared for by a middle-aged son for a time, but this situation became impossible and she was removed to a voluntary home. Re-education started at once and, at first, much against her wishes. She was encouraged to get up and walk about and even to help with minor household jobs. If she had an accident she was made to clear it up herself, and this quickly cured her of incontinence. She became in fact quite a normal old person. Her greatest pleasure was to go to hospital to see her husband and on one occasion I took her myself. When she reached the hospital and she got out of the car, she suddenly found she could hardly walk at all, and had to be more or less dragged in. It was clear that the old attitude was returning with the prospect of seeing her husband, and if he had come back to live with her, she would quickly have relapsed into her old habits.

This is an extreme case, but many old people can be reduced to invalidism if nothing whatever is expected of them.

NURSING OF THE AGED

One of the skills necessary in nursing old people is that of knowing when to leave them in bed, and when

* F. E. Williams' lecture for 1952, delivered before the Royal College of Physicians of London on July 15.

to encourage them to get up and then to move about and go out. The difference in will-power for recovery is always unpredictable. Desire for the adventure of living is easily lost, but can recover to a surprising extent in skilful hands. It depends largely on whether interests have been developed earlier in life. As one woman said, "I have never read a book because I have never had time, but I am told I have missed a rare treat!"

I remember one old woman of ninety who was sent to me by the milkman. He had found her sitting on the pavement tired out with searching for a room. No one would accept her as a tenant for she looked poor, dirty, and ill. She had been offered a place in an institution, but she had said that this was out of the question as she must be able to have access to a library and be able to read. She was found a single furnished room and here she lived for some years completely happy reading Milton, Byron, and Shakespeare, first with both eyes, then with one, and finally, when she became almost blind, she gave up her reading and died.

It is impossible to overemphasise the fact that the function of the hospitals is to cure illness and their equipment is not suited to any other purpose. When no further treatment is possible different conditions than those of the hospital ward are required. There must be some place for chronic patients where there is every incentive for the activities of which they are capable, and for encouragement to be up and about. There is no more dreary sight than rows of chronic sick beds. Prof. A. P. Thomson, of Birmingham, in his report on the *Care of the Chronic Sick*, writes:

"My most vivid impression of the chronic ward of this hospital is an atmosphere of profound apathy. . . . The hospital treatment was surprisingly good . . . the words 'medical treatment' are used in the narrowest sense to signify therapeutic use of rest and drugs."

Most of the inmates of the chronic wards must be regarded as a sad inheritance of a long period of neglect. There are, of course, notable exceptions, but these words describe the lot of thousands of old people in all parts of the country.

It is essential that the most helpless of the chronic sick should be cared for permanently in some kind of hospital, but there is no reason why conditions in some hospital wards should be so deplorable. Years of lying in a ward sometimes amounts to actual cruelty; where, for instance, it is rarely possible to get out of doors, and where there are no decisions to be made, no responsibilities to be accepted. Life is regularised, movement limited to sitting on a chair beside a bed, attired in a dressing-gown, and possessions are almost non-existent. Unfortunately many hospitals have no provision for patients' clothes, even when they remain in hospital for many years. The effect is psychologically bad and not conducive to a return to ordinary living; also from the point of view of geriatric treatment there is little better gentle exercise than that of slowly dressing.

An old woman of my acquaintance suffering from rheumatoid arthritis lived alone upstairs. She managed two small flights of stairs and with a home help succeeded in keeping her home very well. Recently she went to hospital on account of digestive trouble. This quickly cleared up, but she was kept in bed and when sent home at the end of a few weeks she could do nothing for herself and became completely bedridden. Again, an elderly woman came to one of our homes suffering from rheumatoid arthritis. She had been in hospital for $3\frac{1}{2}$ years and, although mentally alert, she had never been dressed, as she had no clothes in hospital, and had therefore never been out. She had most successfully learned to do absolutely nothing, and unfortunately had lost all power or incentive to help herself; she was greedy of one thing only, and that was attention by the nurses to her physical wants, and she assumed a garrulous, demanding attitude to anyone who would attend her.

POSSIBILITY OF BETTER CONDITIONS

There are residential homes where it has been shown that old people who have been rendered immobile by crippling diseases can still find much enjoyment of life. In one such home they are taken for bus-rides, even the very crippled, which resuscitates them more than any physic. They spend much of their time in the garden in summer and have their possessions round them at the cost of tidiness. They go to bed and get up when it suits them, and they are encouraged to occupy themselves in any way possible. All this, incidentally, costs only a third or less of a hospital bed. Although few of these patients can walk out in the road, they have a spirit of gaiety and happiness due to activity of mind even if not of body. A series of very small activities makes all the difference between complete lethargy and liveliness, but all such activities take time on the part of the attendants. Through the overemphasis of safety-first methods, old people are kept in bed for long periods for fear of falls or other accidents. This may be done to save possible censure of the hospital staffs, but it is at the expense of liberty and happiness.

The will to live is the strongest of all instincts and persists in old age. Old people rarely want to die even when life seems to have little to offer. Sometimes fear of death inclines an aged invalid to accept a life involving no sort of effort as the safest means of preserving it. Furthermore, when old persons with an income are cared for by the regional hospital board they contribute nothing for maintenance. Their income can be given to their relatives and this can continue for an unlimited period of time. A return to activity and the resulting transfer from a hospital bed to other accommodation may mean payment of the cost of maintenance. The improvement in health resulting from this change is consciously or unconsciously resisted both by the old people and their relatives. A heavy reward is paid for a continuance of infirmity.

Old people sleep much less at night than younger people and it is acute misery for many of them to lie in bed perhaps up to fifteen hours nightly, sleeping little, listening to the coughing and snoring of their fellows, and waiting for the coming day. Old people are extremely individualistic, and to have any rule by which they must all go to bed and get up at one set time cannot possibly be right. Incontinence alone should rarely be a reason for bedfastness. It may be easier for the nurses to keep them in bed, but it is wonderful how this disability can be managed by experienced and patient attendants. The treatment of incontinence is, indeed, a special science and it is a sign of failure on the part of the nurses when an active-minded patient is restricted to a chronic bed for this reason alone.

Extreme cleanliness and tidiness is of course essential in a surgical ward, but in the wards for the chronic sick the constant struggle for tidiness often results in unintentional but nevertheless cruel discipline. Probably the basis of the whole trouble is that old age and sickness have been for too long confused. Actual skilled nursing, though important, should not be the predominant feature in caring for the aged. Kindliness and resourcefulness should come first, the skilled nursing being reserved for those in real need of it.

The chief difficulty in employing untrained attendants for the chronic sick is their difficulty in lifting the more helpless patients. If they could be taught the best methods, the situation would be greatly eased, since in other respects they can give much of the care required.

Lack of possessions is a sore trial, and the care of even a small assortment of personal treasures gives occupation. Indeed in some cases of mental instability, the arranging and rearranging of possessions is the one steadying influence. I remember one old lady who was getting extremely vague about everything. She tidied her chest of drawers for many hours a day. When it was suggested that so much standing was bad for her and she was prevented from doing it, she became quite violent.

One of the causes of the liability to become bedfast after arrival in hospital or home is the shock which old people suffer from any sort of transference from one place to another. We have observed that on arriving at a strange place this tendency to shock makes them seem much more incapable than they really are. Great patience is needed at this stage to make the change-over easy for them, and where this help is not given they may rapidly break up altogether. This is not always due to a lack of desire for the change, for even when they have chosen this themselves they still seem to undergo mental disturbance for a time after arrival. In bringing people to our homes, we often advise them not to give up their previous dwelling until they have settled in. This gives them the feeling that they have not completely cut away and could, if necessary, still return to their old way of life. Even so we can rarely form any correct estimate of their condition for the first week or two.

With the old there is a special danger of paying too much attention to their physical ills and too little to their mental troubles. Actually disabled old people are still capable of considerable happiness where they are not in bondage to an exaggerated and soul-destroying emphasis on the need for cleanliness of the body and tidiness of surroundings. Mental deterioration is inevitable with unlimited and unoccupied leisure. Chronic inactivity of the mind is even more harmful than that of the body. It is as important to take early steps to prevent disease in the elderly as in any other section of the community although it may require more realisation of the close connection between ills of the mind and body. People are still expected to know by instinct how to look after their ageing relatives as they were once expected to know by instinct how to care for young children.

IMPORTANCE OF COÖPERATION

Since at present accommodation and service are insufficient, it is important for each district to take stock of its resources and use them to the best advantage. Many organisations are not fully used from lack of concerted effort, and because of the difficulties of getting the right people into the right places. Those who are not in need of hospital treatment help to fill the beds; old people die neglected at home because the hospitals and homes for the old have too many people in them who could live in their own homes if flatlets were available for them.

In one area which I know well a great deal of coöperation between all these forces has been achieved. Let us follow the fortunes of an imaginary old lady.

She lives alone and is well known to the Old People's Welfare Committee who have helped her by arranging for meals to be brought to her, and giving useful advice and occasional help in cleaning. She has fallen ill and the doctor cannot get her a bed in hospital and she cannot afford help at night. However, the wheels get moving. In order to admit her to hospital, a convalescent old lady is moved out into a half-way house or convalescent home that has been set up by the King Edward's Hospital Fund; to vacate a bed there, an old lady is moved to a permanent voluntary home; and again in order to find room for her, the local voluntary housing association finds a furnished room or flatlet for an elderly woman who has improved in health and would like to live independently again.

This combined effort is much more effective than isolated action on the part of the hospital, home, or housing trust. The hospital will cease to be wary about taking a temporary patient nor will a home be afraid of taking a frail old lady with whom they might be left when she became bedridden. Not only do these particular organisations work together but they assist and are assisted by the welfare authorities, regional hospital board, and Assistance Board. Mutual goodwill and coöperation can save much effort.

Coöperation is greatly facilitated if, instead of setting up one large institution, several homes are grouped in such a way that residents of various mental and physical grades can be classified and placed together in most congenial surroundings. When there is a change in a patient's condition a shift from one home to another can be made without shock, since the management and atmosphere are so similar throughout and the residents are accustomed to sharing entertainments and excursions.

CONCLUSION

As much understanding and careful management is required for old people as is now afforded for infants and young children. Immense strides may be possible in the next few decades in the reduction of chronic sickness in old age, and these may be as dramatic as the recent drop in infant mortality. There are few more miserable sights than a ward of chronic sick invalids, and few more depressing occupations than their care. **Robert Burton** once said: "There is no greater cause of melancholy than idleness"; and we might add—no greater cause of ill health than melancholy.

CONVERSION OF TISSUE POLYSACCHARIDES TO AUTO-ANTIGENS BY GROUP-A BETA-HÆMOLYTIC STREPTOCOCCI

L. E. GLYNN, M.D. Lond., M.R.C.P.
DIRECTOR OF PATHOLOGY

E. J. HOLBOROW, M.A., M.B. Camb.
RESEARCH BACTERIOLOGIST, SPECIAL UNIT FOR JUVENILE RHEUMATISM

CANADIAN RED CROSS MEMORIAL HOSPITAL, TAPLOW, BUCKS

THE ætiology of nephritis and the rheumatic diseases is still unknown, but many workers have suggested an antigen-antibody reaction as a possible mechanism (e.g., Klinge 1933, Rich and Gregory 1943, Hawn and Janeway 1947). Although lesions resembling in various degrees those of the corresponding human disease have been produced in laboratory animals by the injection of massive doses of foreign protein, this artificial procedure can only serve as a remote analogy to the sequence of events in the naturally occurring disease. It has seemed possible, however, to many investigators that specific antibody production in response to the individual's own tissues (acting as antigen) may be involved, rather than a non-specific antigen-antibody reaction induced by foreign material (Smadel 1936, Cavelti and Cavelti 1945). Unfortunately for this hypothesis, the experimental production of auto-antibodies has proved extremely difficult, although a-priori evidence of the possibility exists in the acquired hæmolytic diseases (Loutit and Mollison 1946).

In rheumatic fever (and to a lesser extent in nephritis) recent infections with hæmolytic streptococci are accepted as an essential ætiological factor. It has been suggested that the effect of these is to render the tissues auto-antigenic. The claim of Cavelti and Cavelti (1945) to have utilised this mechanism in the experimental production of nephritis and carditis has not, however, been confirmed (Humphrey 1948).

The classical work of Landsteiner (1945) has shown that the antigenicity of a protein may be profoundly altered by chemical combination with various non-protein substances (haptenes). Among the latter the polysaccharides are of outstanding importance in conferring specificity on bacterial antigens (Heidelberger and Avery 1923, 1924, Avery and Heidelberger 1923, 1925). A possible mechanism, therefore, for auto-antibody stimulation would be the combination between bacterial protein and tissue polysaccharide, acting as haptene. The work of Morgan and Partridge (1940) on the structure of the somatic antigen of *Shigella shigæ* has well shown that the protein moiety of this antigen can readily combine with

polysaccharides such as agar and cherry gum to produce antigens capable of eliciting antibodies reacting specifically with the corresponding polysaccharide. It has been shown by Sordelli and Mayer (1931) that this property is by no means confined to dysentery organisms, and we have recently reported that hæmolytic streptococci are particularly active in endowing with antigenicity various polysaccharides of plant origin (Glynn and Holborow 1952). If it can be shown that these organisms can similarly react with polysaccharides of animal connective tissue, it is conceivable that the production of auto-antibodies to these tissue polysaccharides might occur in natural infections. Such a reaction could well underlie the pathogenesis of the group of diseases under discussion.

We report here results of such experiments, in which a preparation of chondroitin sulphate was used as tissue polysaccharide; a limited quantity only was available for this experiment, which was therefore restricted in scope. A note is also included on the production of nephritis in rats, using a tryptic digest of rat kidney as a source of kidney polysaccharide.

METHODS

Chondroitin sulphate * was prepared from stored wet human costal cartilage by the method of Einbinder and Schubert (1950) as a dry powder, readily soluble in saline solution.

Preparation of vaccines.—18-hour cultures in Todd Hewitt broth of a group-A type-4 strain of β-hæmolytic streptococcus were centrifuged, and vaccines prepared from the organisms washed twice in saline solution. The live cocci were suspended in a small volume of 1% chondroitin-sulphate solution in saline solution and kept at 37°C for an hour. They were next centrifuged, washed twice, and resuspended in saline solution to give an opacity equivalent to about 1000 million cocci per ml., and killed by heating at 56°C for thirty minutes. Control vaccines were prepared identically but without the chondroitin sulphate.

Immunising procedure.—Young cross-bred Dutch or Copenhagen rabbits, weighing 1·4–1·8 kg. and kept in individual cages on a mixed diet, were given intravenous injections of vaccine three times a week. On a dosage beginning with 0·5 ml. and increasing to 1·0 ml., and given a vaccine prepared in bulk at the outset of the experiment (schedule A), a high proportion of rabbits died or sickened after two or three doses. On a reduced dosage (starting with 0·1 ml. and gradually increasing to 1·0 ml.) and given freshly prepared vaccine for each injection (schedule B), the rabbits remained well during the initial stages of the immunising course.

Two Copenhagen rabbits received intracutaneous inoculations of chondroitin-treated vaccine in six daily doses of 0·1 ml. Three control rabbits received chondroitin-free vaccine, or chondroitin-sulphate solution only, intracutaneously.

Tests for precipitating antibody to chondroitin sulphate.—Sera were obtained from the rabbits at intervals and tested for precipitin reaction with 0·1% chondroitin-sulphate solution in saline solution. Ring tests, chondroitin solution being layered on serum, were unsatisfactory owing to the slow rate of appearance of precipitate, and precipitation was best observed in capillary tubes, as in the technique described by Swift et al. (1943) for streptococcal precipitin typing. Equal quantities of serum and chondroitin solution were drawn up into a capillary tube and incubated at 37°C for two hours. With positive sera maximal flocculation was observed after refrigeration at 4°C for up to forty-eight hours. Normal rabbit sera gave no trace of precipitation with the polysaccharide solution under these conditions.

Streptococcus-kidney-digest vaccine.—A tryptic digest of perfused rat kidney was prepared by the method of Cole et al. (1951) and a streptococcus-kidney-digest vaccine made in the same way as the vaccines described above.

* Kindly supplied by Dr. Gerald Loewi.

RESULTS

Antigenicity of Chondroitin-sulphate Preparation Alone

A solution of chondroitin sulphate alone gave rise to no precipitins when injected intravenously—e.g., 60 mg. given over twelve days. Repeated intracutaneous injection over eight days (6×0·1 ml. of a 1% solution) did not cause skin sensitivity in two rabbits.

Antigenicity of Streptococcus Alone

Plain streptococcal vaccine gave rise to no chondroitin-precipitating antibody in the three rabbits immunised.

Antigenicity of Streptococcus-chondroitin Vaccine

Intravenous immunisation.—Six rabbits received intravenous streptococcus-chondroitin vaccine; four according to schedule A, and two according to schedule B. The sera obtained from these rabbits after immunisation all gave precipitation with chondroitin solution, varying from a trace to a ++ reaction (see table). One of these rabbits developed a limp in the left hind leg after fourteen days and was killed on the sixteenth day. Its serum gave a relatively strong precipitin reaction with chondroitin-sulphate solution. Post mortem the left knee-joint showed acute inflammation but was sterile on culture. The synovial membrane was œdematous and injected, and there was much hyperæmia round the articular margins. Another rabbit showed no clinical symptoms but died on the twenty-third day of schedule B. Serum obtained at this time precipitated strongly with chondroitin-sulphate solution, and post mortem both knee-joints showed much œdema and inflammation of the synovial membrane. As shown in the table, histological evidence of arthritis was obtained in five of the six rabbits receiving the streptococcal-chondroitin vaccine. In one this consisted of a slight infiltration with poly-

PRECIPITIN REACTIONS WITH CHONDROITIN-SULPHATE SOLUTION OF RABBIT ANTISERA TO STREPTOCOCCUS-CHONDROITIN VACCINE

Immunising agent	Rabbit no.	Total dosage (ml.)	Period of experiment (days)	Fate of rabbit	Precipitation of rabbit sera with $Ch.SO_4$	Joint lesions
Streptococcus-chondroitin: Schedule A	21/2	4	7	Died	Trace	..
,,	21/2A	5	16	Killed	++	Acute synovitis
,,	21/2B	3·5	9	Died	+	Slight polymorph infiltration
,,	23/4	2	7	Killed	Trace	Acute synovitis
Schedule B	23/3	4	18	Died	+	Severe acute synovitis
,,	23/4A	6·5	23	Died	++	Subacute synovitis
Chondroitin solution only (1%)	21/4	6	14	Survived	0	..
,,	21/5	6	14	Survived	0	..
Streptococcus only: Schedule A	23/1	3·5	30	Died	0	Normal
,,	23/2	2·0	7	Died	0	An occasional polymorph
Schedule B	23/2A	7	26	Killed	0	Normal

Precipitin reaction after 48 hr. at 4°C: trace, fine deposit; +, small aggregates in deposit; ++, large aggregates in deposit.

morphs; in two others there was considerable hyperæmia, with polymorph infiltration; in the fourth the inflammation was intense and acute; and in the fifth it was severe, but polymorphs were few, the predominant cells being lymphocytes and plasma cells forming well-marked perivascular aggregations. Cultures taken from all the joints examined were invariably sterile. No comparable degree of inflammation was found in any of the controls; in one rabbit only a slight polymorph infiltration was present.

Intracutaneous inoculations.—Of the two pairs of rabbits inoculated intracutaneously one member of each pair received streptococcus-chondroitin vaccine and the other received the streptococcus alone. Six daily injections were given in the skin of the flank, and skin tests with 0·1 ml. of 1/1000 chondroitin sulphate were made after an interval of five days. Considerable skin sensitivity to chondroitin was elicited in the rabbits receiving streptococcus-chondroitin vaccine; negative results were obtained with the rabbits receiving streptococcus only. The positive skin reaction obtained was of the delayed type, appearing at about six hours, and maximal at twenty-four to thirty-six hours, taking two days to fade.

Experiments with Rat-kidney Digest

A rabbit antiserum to the streptococcus-kidney-digest vaccine was obtained, which when given intravenously to rats gave rise in twenty-four hours to gross albuminuria and to glomerular lesions in the kidney comparable to those induced in a parallel experiment by nephrotoxic serum (Smadel 1936). Normal rabbit serum or plain antistreptococcal rabbit serum produced no lesions or albuminuria.

DISCUSSION

It is evident from these results that the production of antibodies to polysaccharides of animal origin can be induced in the same way as those previously obtained against polysaccharides of plant origin. We cannot regard the haptene in these experiments as strictly autogenous, since the chondroitin was obtained from human cartilage; but there is little evidence that the composition of this material varies from species to species. It will, of course, be necessary in repeating these experiments to use chondroitin prepared from cartilage of the homologous species. A point of great interest relates to the extremely minute quantity of polysaccharide necessary to impart its own immunological specificity to the streptococcus. For example, with electrophoretic methods capable of detecting a few microgrammes of galactose, it has been impossible to detect even a trace in 2 mg. of dried cocci, previously treated with agar, although vaccines prepared from these readily elicited antibody to agar. Figures for the purity of the chondroitin sulphate are unfortunately not available; its N content, however, was only 2·2–2·4%. Since chondroitin sulphate has an N content of less than 3%, other protein could not have been present in more than traces. This is confirmed by the absence of antigenicity of the polysaccharide solution alone.

Of the six rabbits injected with the streptococcus-chondroitin the two showing strongest serum precipitation showed also the most conspicuous joint lesions. Less severe lesions were also present in two of the rabbits showing less precipitation. This does not necessarily imply that the lesions are due to the antibodies responsible for the precipitation reaction; it is quite conceivable that, if antibodies are responsible for the lesions, they belong to the non-precipitating type. It does, however, suggest that lesions are most likely to occur in those animals with the most responsive antibody mechanisms.

As already mentioned, the scope of these experiments has been limited by the small quantity of animal polysaccharides available in a relatively pure and undegraded state, and we hope to confirm and extend these observations with more polysaccharide material.

SUMMARY

A vaccine prepared from group-A β-hæmolytic streptococci in the presence of chondroitin sulphate gave rise to rabbit antisera precipitating with this polysaccharide.

Of six rabbits immunised with such a vaccine five showed macroscopical and/or microscopical evidence of joint lesions. Control rabbits receiving either streptococci or polysaccharide alone showed no joint lesions apart from an occasional polymorph in the synovial membrane.

We acknowledge with pleasure the advice and interest of Dr. E. G. L. Bywaters and the biochemical advice of Dr. R. Consden.

REFERENCES

Avery, O. T., Heidelberger, M. (1923) *J. exp. Med.* **38**, 81.
— — (1925) *Ibid*, **42**, 367.
Cavelti, P. A., Cavelti, E. S. (1945) *Arch. Path.* **39**, 148; **40**, 158, 163.
Cole, L. R., Cromartie, W. J., Watson, D. W. (1951) *Proc. Soc. exp. Biol., N.Y.* **77**, 498.
Einbinder, J., Schubert, M. (1950) *J. biol. Chem.* **185**, 725.
Glynn, L. E., Holborow, E. J. (1952) *J. Path. Bact.* (in the press.)
Hawn, C. V., Janeway, C. A. (1947) *J. exp. Med.* **85**, 571.
Heidelberger, M., Avery, O. T. (1923) *Ibid*, **38**, 73.
— — (1924) *Ibid*, **40**, 31.
Humphrey, J. H. (1948) *J. Path. Bact.* **60**, 211.
Klinge, F. (1933) Der Rheumatismus. Munich.
Landsteiner, K. (1945) The Specificity of Serological Reactions. Harvard and London.
Loutit, J. F., Mollison, P. L. (1946) *J. Path. Bact.* **58**, 711.
Morgan, W. T. J., Partridge, S. (1940) *Biochem. J.* **34**, 169.
Rich, A. R., Gregory, J. E. (1943) *Bull. Johns Hopk. Hosp.* **72**, 65.
Smadel, J. E. (1936) *J. exp. Med.* **64**, 921.
Sordelli, A., Mayer, E. (1931) *C.R. Soc. Biol. Paris*, **107**, 736.
Swift, H. F., Wilson, A. T., Lancefield, R. C. (1943) *J. exp. Med.* **78**, 127.

DEFORMING FACTORS IN THE EARLY STAGE OF POLIOMYELITIS

G. P. MITCHELL

M.C., M.B. Aberd., F.R.C.S.E.

SENIOR REGISTRAR, WINGFIELD-MORRIS ORTHOPÆDIC HOSPITAL, OXFORD

From the Nuffield Orthopædic Centre, Oxford

THE term "muscle spasm" has often been used to describe various types of muscle dysfunction in poliomyelitis, but there does not seem to be any general agreement on its definition and cause.

Pohl and Kenny (1943) consider muscle spasm to be a decisive factor in the course of poliomyelitis. Pollock et al. (1949), on the other hand, deny the existence of muscular spasm, which they define as a state of sustained involuntary tetanic contraction of muscle—a definition with which I agree. Excluding the types of muscular spasm attributed to the meningeal reaction, they found no evidence of true spasm in patients studied during the first ten days of poliomyelitis.

Because of the existing controversy I have tried here to describe more accurately the various clinical findings which are sometimes collectively described as spasm, and to discuss their ætiology.

DEFORMING FACTORS

In patients who have had little or no treatment in the early months of poliomyelitis, deformities are occasionally found which seem to be due to abnormal overaction of unaffected or mildly paralysed muscle groups. It is therefore essential to study the factors concerned in the limitation of passive mobility in the first few weeks of the disease. Deformities appearing later, which are due to neglect of a paralysed limb or to the influence of simple muscle imbalance on growth, will not be discussed.

For the present purpose the term "deforming factors" is used to describe any conditions which interfere with the passive mobility of the limbs in the early stage of poliomyelitis. The observations are based on the study of over 100 cases examined during the isolation-hospital stage and subsequently in the orthopædic hospital.

VOL

TIGHTLY

BEST C

AVAIL

LUME

BOUND

COPY

ILABLE

Deforming factors appear to be manifested in three ways: (1) limitation of straight leg raising; (2) limitation of shoulder abduction beyond 80°; and (3) muscle resistance to stretch. These conditions do not all necessarily proceed to established deformities if untreated.

Limitation of Straight Leg Raising

The limitation of straight leg raising referred to here is that persisting after the initial acute meningeal reaction has subsided. When present to any great extent it persisted for many weeks and could not be completely abolished by treatment in the early stage, but improved in the later stages on mobilisation of the patient, particularly by walking and sitting.

In severe cases pain was produced when the leg was raised to an angle of 30°, accompanied by painful resistance to stretch of the hamstrings when these muscles were not paralysed. Where the muscle on one leg was considerably weaker than that on the other, there was only a minor difference in the angle obtained. Even when complete paralysis affected the hip and leg, straight leg raising was limited by pain often to 30° unaccompanied by muscle resistance.

The limitation of straight leg raising was always bilateral and not necessarily proportional to the degree of paresis, but was not present unless there was some paralysis of the leg.

In these patients the hip-joints were mobile and could be flexed to over 90°. All the patients had lumbar pain in the early stages, and several had neck stiffness, but severe degrees of neck stiffness were often unaccompanied by any limitation of straight leg raising.

Limitation of Shoulder Abduction

This was an outstanding feature in the few patients presenting severe degrees of resistance to muscle stretch in the biceps and shoulder adductor muscles. It was also present in patients with respiratory weakness, when the pectorals were used as accessory muscles of respiration.

Limitation of shoulder abduction persisting after the initial meningeal phase was found in many patients with paralysis affecting the arms. Pain was produced on abduction beyond 80°, accompanied by strong resistance in the shoulder adductor muscles when these were active. It was only seen where the arm or the trunk was affected, and was bilateral in severe cases. Neck stiffness was a feature of the febrile stage in these patients. When the shoulder was abducted to a few degrees below the pain-producing angle, pain could be produced by lateral flexion of the neck to the opposite side.

This limitation of shoulder abduction was more easily overcome than the limitation of straight leg raising.

Muscle Resistance to Stretch

A state of sustained tone or "spasm" in the muscles of the neck and back was often observed during the meningeal reaction of the first few days in both paralytic and non-paralytic cases. This sustained tone disappeared as the fever subsided, but was sometimes followed by muscle resistance to stretch, which developed on attempted flexion of the spine. This muscle resistance gradually subsided over a longer period.

As has been mentioned, muscle resistance to stretch developed in the hamstrings during the straight-leg-raising test and in the shoulder adductor muscles during the shoulder-abduction test. This resistance was only present when the muscle was able to contract, and it was therefore considered to be a secondary phenomenon.

In a few patients considerable muscle resistance to stretch was noticed in certain muscles, particularly the biceps, when the elbow was held in a flexed position and any attempt at extension initiated contraction at about 90°. This was considered to have a more complex ætiology than the muscle resistance mentioned in the preceding paragraphs, and was considered to be a significant deforming factor if untreated. For this reason it will be discussed under a separate heading.

This type of increase in muscle tone in the extremities was an infrequent finding. In 100 patients treated from the onset by the methods in use at Oxford and previously described by me (Mitchell 1952), 4 patients showed significant muscle resistance to stretch of a degree likely to persist if untreated. The biceps muscle was affected in 3 cases, and the calf muscles in 1 case; 2 other patients developed biceps resistance during the respirator stage of the illness. No example of true spasticity was found; clonus and increased tendon-reflexes were not obtained. Observation at the onset did not reveal any muscle contraction in the limbs when at rest; this state was brought on by any attempt to stretch the muscle and was accompanied by pain. The term "muscle resistance to stretch" is preferred to the more common term "spasm" in describing the muscle dysfunction.

The muscles usually affected were the elbow flexors, adductors of the shoulder, and calf muscles. If such a muscle is allowed to remain in a position of advantage, the temporary state of resistance by contraction is gradually superseded by shortening, the muscle being felt as a tight cord under general anæsthesia in contrast to the relaxation obtained in the early stage.

CLINICAL OBSERVATIONS

In an attempt to explain these changes in the cases we have examined, the clinical features only will be discussed, no necropsy material being available.

Limitation of Straight Leg Raising

As has been mentioned, in these cases the hip-joints were mobile and could be exonerated. The degree of muscle power present did not materially affect the angle of straight leg raising obtained, which was severely limited even when muscle power was minimal or absent. The limitation was caused by muscle resistance to stretch plus pain where muscle power was good, and by pain alone when muscle power was absent. Intravenous thiopentone was given in 1 case with persistent limitation of straight leg raising six weeks after the onset. Under anæsthesia the straight-leg-raising angle was increased from 30° to 90°, showing that permanent shortening of the muscle had not taken place. It was not thought justifiable to paralyse the muscle, since Schlesinger (1951) found that limitation and pain persisted even with muscles rendered atonic with intravenous mephenesin. It is unlikely that brain-stem lesions were responsible for the limitation where muscle power was unequal or absent. Muscle resistance to stretch, when present, did not correspond to the spasticity seen in proved traumatic brain-stem lesions. Lasègue's sign was positive in all cases where limitation was severe.

The most likely site of lesions causing pain and limitation on attempted straight leg raising was considered to be in the region of the meninges and dorsal roots. The backache and limb pains of the early stage were considered attributable to inflammatory lesions at this site. The clinical picture in the early stage closely resembles certain cases of intervertebral-disc protrusion.

Limitation of Shoulder Abduction

Limitation of shoulder abduction over 80° was seen less often than the leg limitation, but certain features were similar. It was always accompanied by some degree of upper-limb paralysis—the abduction limit was caused by pain where muscles were paralysed, and by pain plus muscle resistance to stretch where power was present. Possibly the limitation and neck stiffness could also be due to changes in the region of the dorsal roots and meninges.

Muscle Resistance to Stretch

This was only a transient complication when cases were treated from the onset by rest, sedation, gentle passive movements, selective positioning, and splintage. Advanced cases were seen where inadequate early treatment had been given. The muscle resistance was usually bilateral and occurred in slightly affected or apparently normal muscles. The flexor adductor groups of the arm were more commonly affected, particularly the biceps, any attempt to extend the elbow being opposed by strong contractions. Patients with much biceps resistance possessed highly emotional temperaments. Pain was a noticeable feature in all the cases.

Several factors were considered to contribute to the state of muscle resistance to stretch as seen in these patients: (1) incoördination of muscle action caused by internuncial lesions; (2) overaction of muscle, either deliberate or from emotional tension; and (3) limb pain.

(1) *Incoördination of muscle action* in the early stage was found in many patients. Kabat and Knapp (1944) attribute this to the internuncial lesions.

(2) *Overaction of muscle.*—Continued overaction of a stronger over a weaker muscle could cause fatigue and aggravate pain; if untreated, this might progress to shortening and resistance to stretch of the stronger muscle.

An example of deliberate overaction of partially affected muscles progressing to actual muscle shortening was found in a female patient with paralysis of all limbs and trunk. While in the respirator she developed considerable limitation of shoulder abduction owing to the continued use of the pectoral and latissimus dorsi muscles as accessory muscles of respiration. During her periods out of the respirator adjustable wooden wedges were inserted between arm and thorax and adjusted to the greatest comfortable abduction. By this means abduction was gradually improved and eventually a useful range obtained without interfering with the accessory action of the pectoral muscles.

Disproportion in strength between protagonists and antagonists does not necessarily produce deformity; therefore aggravating factors must be present: either deliberate and continued overaction as in the case described, or emotional overaction from prolonged tension in the muscle of a highly emotional patient, when a strong biceps predominates and unrestricted use of the limb in the supine position is allowed. The prevention and ease of correction of such a flexion deformity in the early stage suggests that functional overaction may play some part in its production, perhaps by aggravating the dysfunction produced by pain and incoördination.

A typical example of biceps resistance was in an adult male R.A.M.C. orderly, who was very concerned about the outcome of the disease. He developed biceps resistance on passive extension of the elbow beyond 90°. After a few days' treatment, by engaging him in conversation, the elbow could be passively extended. On drawing his attention to the elbow, however, the muscle resistance reappeared. Later the resistance completely disappeared, but it is of interest, in connection with the other phenomena, that he had pain on abducting the shoulders beyond 80°, and that straight leg raising was limited to 30°, with a positive Lasègue sign. This patient also had a partial lower-limb paresis.

Deformities due to hysterical contracture of muscle were seen in a female patient admitted six weeks after an illness originally diagnosed as poliomyelitis. It was stated that she had developed complete flaccid paralysis of the left arm and leg, but that subsequently "muscular spasm" had appeared and produced deformities. On admission it was noted that an increase in tone and resistance to stretch was present in both flexor and extensor muscles of the left arm and leg. The elbow was maintained in acute flexion and the hand in the "main accoucheur" position. The knee was held in full extension and the foot in equinovarus. Tendon-reflexes were increased in the leg, and Babinski's sign was negative.

(3) *Pain* was present in all the cases of muscle resistance to stretch. After generalised limb pains had subsided, pain occurred only on attempted active or passive movement of the limb. Muscle biopsies in man have failed to show any significant pathological change in the muscles (Clawson 1948, Jungeblut 1950). The site of pain must therefore be between the myoneural junction and the dorsal roots. Inflammatory changes have been found at necropsy in the region of the dorsal roots and meninges (Bodian 1948). Possibly the increased resistance to stretch in muscles such as the upper-limb flexor adductor groups could be an exaggerated muscle guarding in response to pain originating in the dorsal roots or meninges, contributory factors being incoördination resulting from internuncial neurone lesions and emotional overactivity of muscle.

Recently two patients were seen who demonstrated mild muscle-movement resistance of special interest and similarity. Both were healthy adult males of stable mental make-up. The muscle resistance was of minor degree and only present for a few days, after which it completely disappeared. In both cases there was some connection with movements of the cervical spine and the production of muscle resistance.

The first patient on examination showed a mild tendency to biceps stretch resistance which was easily overcome. The shoulder was then passively abducted to 100°, when the patient complained of pain radiating down the forearm, and the biceps contracted, resisting full extension by 30°. When the arm was brought down to the side, the pain and biceps contraction disappeared. When the arm was brought down to just below the pain-producing angle, the pain could be reproduced by lateral flexion of the neck towards the opposite side—this latter sign has since been found in several patients with limitation of upper-limb abduction but was not looked for in previous cases.

The second patient, who was reported as tending to develop deformities, had been propped up in bed with pillows because of respiratory difficulty. He had severe neck stiffness, and overaction of the biceps and shoulder adductors maintained his arms flexed and adducted. When he was placed supine, all the resistance in the muscles disappeared, allowing a full range of passive movements. The neck stiffness disappeared the following week.

CONCLUSIONS

The limitation of straight leg raising and shoulder abduction is considered to be due to pain arising from residual inflammatory changes in the region of the dorsal roots or meninges. In these cases muscle resistance to stretch is guarding in nature.

The greater resistance to stretch found occasionally in muscles such as the biceps cannot be explained by a guarding action alone. Muscle incoördination plus emotional overactivity of a strong or relatively unaffected muscle over a weaker affected muscle may exaggerate the underlying guarding mechanism.

These conclusions have been reached from clinical observations, and I agree with the opinion of Magoun and Rhines (1947) that "further investigation of the pathophysiology of spasm in poliomyelitis would appear necessary before it can be stated definitely to be either an exaggerated stretch reflex or tension maintained reflexly or voluntarily in response to pain or to have some as yet unanticipated etiology."

SUMMARY

Deforming factors appearing in the early stage of poliomyelitis are defined as: (1) limitation of straight leg raising; (2) limitation of shoulder abduction; and (3) muscle resistance to stretch.

Clinical observations are reported which suggest that pain is the main cause of the onset of deforming tendencies in the early stage. Resistance to stretch is guarding in nature. Incoördination and emotional overactivity or tension in a muscle may play a part in the production of the more severe deformities.

I am indebted to the staffs of the Slade Isolation Hospital, Oxford, the Abingdon Isolation Hospital, and the Wingfield-

Morris Orthopædic Hospital for their help and encouragement. I wish to express my appreciation to Prof. J. Trueta and Mr. J. C. Scott for criticism and advice in the preparation of this paper.

REFERENCES

Bodian, D. (1948) *Proc. int. Conf. Poliomyelitis*, p. 62.
Clawson, B. J. Cited by Bell, E. T. (1948) *Ibid*, p. 135.
Jungeblut, C. W. (1950) *J. Pediat.* **37**, 109.
Kabat, H., Knapp, M. E. (1944) *Ibid*, **24**, 123.
Magoun, H. W., Rhines, R. (1947) Spasticity. Springfield, Ill.; p. 27.
Mitchell, G. P. (1952) *Brit. med. J.* i, 649.
Pohl, J. F., Kenny, E. (1943) The Kenny Concept of Infantile Paralysis and its Treatment. Minneapolis.
Pollock, L. J., et al. (1949) *Arch. Neurol. Psychiat.* **61**, 288.
Schlesinger, E. B. (1951) *Ibid*, **66**, 600.

SALT-LOSING NEPHRITIS

C. L. JOINER
M.D. Lond., M.R.C.P.
ASSISTANT, DEPARTMENT OF MEDICINE, GUY'S HOSPITAL MEDICAL SCHOOL, LONDON

M. G. THORNE
M.B. Camb., M.R.C.P.
MEDICAL REGISTRAR, GUY'S HOSPITAL, LONDON

THE importance of maintaining the sodium and chloride reserves of the body and of recognising the clinical features resulting from the deprivation of salt as opposed to water was emphasised by McCance (1936) and again by Marriott (1947). Marriott pointed out that sodium depletion presented an easily recognisable syndrome, whose prominent features are weakness, fatigue, giddiness, fainting, muscular cramps, anorexia, nausea and vomiting, and, later, hypotension and coma.

Sodium occurs so plentifully and widely that inadequacy is seldom the result of a simple deficiency of intake, unless it is due to a salt-free diet too strictly prescribed or too conscientiously followed and aggravated perhaps by the sodium diuresis induced by mercurial drugs (Soloff and Zatuchni 1949). A more common cause of a low sodium state is excessive loss, either from the skin by sweating or from the alimentary tract by vomiting, diarrhœa, or fistulæ. Finally, too much sodium and chloride may be excreted by the kidneys. This loss may be the result of functional changes in the renal tubules, when a deficiency of adrenal cortical hormones induces failure of tubular absorption, as in Addison's disease; or when, as in certain chronic illnesses, in the absence of any apparent renal lesion the ability to retain sodium and chloride is impaired (Winkler and Crankshaw 1938). It is evident also that an addisonian picture could, in theory, result from disease of the renal tubules. Although Peters et al. (1929) described excessive urinary loss of chlorides in certain cases of nephritis, Thorn et al. (1944) were the first to demonstrate what they called "salt-losing nephritis" as a clear clinical picture.

These workers described two cases, both young adults without previous history of renal disease. One was admitted to hospital in a drowsy state, collapsed (blood-pressure 64/46 mm. Hg), vomiting, and suffering from cramps; the other was nearly comatose (blood-pressure 35/0 mm. Hg). In both cases the sodium and chloride levels were grossly lowered in the serum and normal in the urine. Neither patient was pigmented, but adrenal cortical failure was diagnosed because no cells or casts were found in the urine of either, and only a trace of albumin in one. Treatment with large doses of deoxycortone acetate and adrenal cortical extract was ineffective, however, and only the administration of sodium chloride corrected the addisonian symptoms and raised the blood-pressure. The salt-losing tendency appeared to be a transient phase in the disease, and later it ceased, the patients finally succumbing in 2 and 4½ years from uræmia and hypertensive heart-failure. At necropsy the kidneys in both cases were reported to show the changes of chronic nephritis, while the adrenals were quite normal.

Only four other cases of salt-losing nephritis have been described (de la Balze and Oñátivia 1947, Borst 1950, Sawyer and Solez 1949, and Nussbaum et al. 1952). In addition Rosenheim (1951) referred to this disorder and briefly cited another possible case. Nevertheless it is possible that similar cases have been reported previously as examples of Addison's disease with hypertension or Addison's disease complicated by chronic nephritis, particularly when such diagnoses have not been confirmed at necropsy. We acknowledge the undoubted authenticity of certain of these cases of combined renal and adrenal failure, however (Ravreby and Sawyer 1948).

We have found no original descriptions of this condition in the literature of this country, but it has been the subject of an annotation (*Lancet* 1952). In presenting a further three cases, therefore, we hope to draw attention to an important differential diagnosis of Addison's disease and one whose treatment should, in most cases, be at least temporarily rewarding. Case 1 reported here cannot be considered to be established beyond doubt and is presented as being of historical interest, for, although the disease was not proved to be a salt-losing one, the account of the clinical and pathological findings accord well with the original description of Thorn et al. (1944). All three cases were investigated and treated at Guy's Hospital.

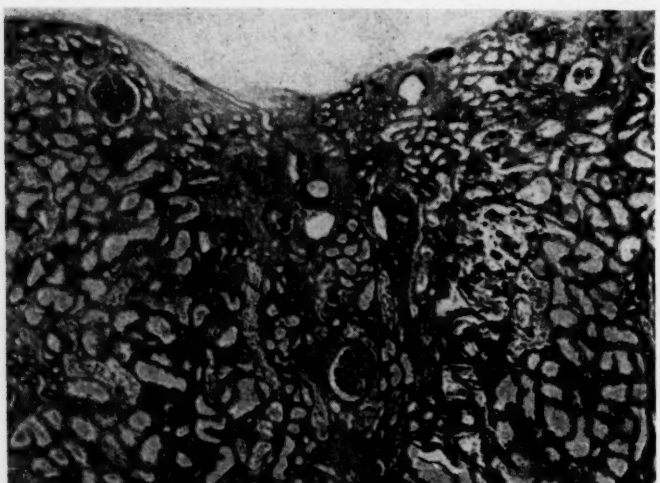


Fig. 1—Depressed cortical scar, tubular dilatation, and glomerular sclerosis of chronic pyelonephritis (case 1). (Van Gieson × 24.)

CASE-RECORDS

Case 1.—A girl, aged 20, was admitted on June 30, 1930, under the care of Dr. John Ryle. She complained of being easily tired, "slack," weak, and irritable since an attack of influenza two years previously. She had noticed bronzing of the skin for about a year, and amenorrhœa for 4 months. Until the age of 17 she had had nocturnal enuresis and since then had had considerable frequency by day and night. At the age of 9 months she had had pneumonia, and at the age of 13 months scarlet fever and diphtheria. She had had other childhood ailments, including two operations on tonsils and adenoids. One sister had recently died from tuberculosis.

On examination she weighed 6 st. 4½ lb. and appeared somewhat younger than her

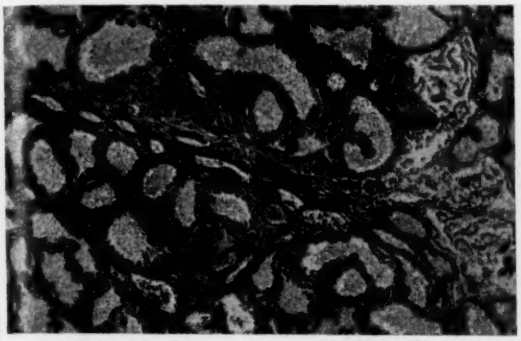


Fig. 2—Calcification of basement membrane of hypertrophied and dilated tubules (case 1). (Von Kossa × 74.)

years. Her skin was "bronzed," and her nipples were deeply pigmented. There was additional darkness over pressure points, and some small pigmented spots were seen in her mouth. Her blood-pressure was 100/70 mm. Hg., but no abnormality was detected in any other system. Her urine, sp. gr. 1·016, showed a trace of albumin. A blood-count showed Hb 7·2 g. per 100 ml., red cells 2,650,000 per c.mm., colour-index 0·92, and white cells normal. A test-meal was likewise normal. Radiography of the chest showed infiltration at the right apex. Dr. Ryle thought her condition most like that seen in Addison's disease.

Progress.—The patient rapidly deteriorated, and by July 9 was much worse, complaining of great lassitude and malaise, and her blood-pressure was 79/57 mm. Hg. On July 10 she was almost comatose, her reflexes being only just obtainable, and her pupils reacting poorly to light. Her blood-pressure then was 69/48 mm. Hg. By the afternoon she became unconscious, her pupils ceased to react to light, and shortly after this she died.

Necropsy findings.—Both adrenal glands were large and completely healthy. The kidneys were small (18 g. and 31 g.) and the capsules stripped easily, showing a mottled surface with some depressed scars. Section showed that the cortex was narrowed to 9–10 mm., and the corticomedullary junction ill differentiated. The skull was thickened and soft, resembling that seen in Paget's disease. Some tuberculous infiltration was found at the apex of the right lung. The other organs were normal, the parathyroid glands not being noted to be enlarged. On histological examination (Dr. J. B. Enticknap) the kidney changes were seen to be those of healed pyelonephritis (fig. 1), with evidence of a recent exacerbation. Calcification was seen in the tubules (fig. 2). The adrenal glands were of normal structure.

Case 2.—A man, aged 27, was admitted on July 27, 1951, with several weeks' history of weakness and tiredness and about 6 hours' history of pain in the left loin and inability to micturate. His family history was irrelevant. At the age of 18 months he had a tuberculous gland excised from his neck. At the age of 20 years his right kidney was found to be tuberculous and was subsequently removed surgically. At that time his blood-pressure was 150/90 mm. Hg and some impairment of renal function was noticed even postoperatively, the blood-urea remaining raised at 48 mg. per 100 ml. in July, 1945, and 60 mg. in February, 1946. He continued to pass tubercle bacilli in his urine. In 1948, at the age of 25, miliary tuberculosis of the lungs was discovered and treated with streptomycin and rest, with good result, but the blood-urea level reached 200 mg. per 100 ml. at this period. There was a decline from this high level, but shortly before admission to hospital in 1951 it still stood at 120 mg.

On examination the patient was thin but of good colour. His blood-pressure was 115/80 mm. Hg, and the only significant physical abnormalities detected were pyrexia (103°F), pulse-rate 100, and tenderness on palpation of the left loin. His urine, however, contained protein 2 g. per litre besides pus cells and acid-fast bacilli.

Progress.—The pain in the loin subsided within a few hours, and the patient micturated freely. Within 3 days his temperature had fallen to normal, but a week after his admission there was a bout of anuria lasting nearly 24 hours. Even before this his general condition started to deteriorate. Cramps developed in his legs and hands, his appetite was poor, and he was weak, listless, and at times faint. His blood-pressure dropped but did not reach the levels seen in addisonian crisis, the systolic pressure never falling below 100 mm. Hg. Estimations of the serum-electrolytes now revealed a gross depletion of sodium, at 266 mg. per 100 ml. (115 m.eq. per litre), and of chlorides at 396 mg. per 100 ml. (114 m.eq. per litre), while the blood-urea level was considerably raised. Although the tongue and skin were dry and he vomited occasionally, he continued to pass considerable quantities of urine of a very low specific gravity, which nevertheless contained relatively large quantities of sodium chloride (see table). Treatment with sodium chloride by mouth was started, and later, because he did not tolerate this well, large quantites of physiological saline solution were given per rectum and intravenously. On the 14th day after admission, the serum-sodium level still being grossly depressed, the patient was given intramuscular injections of 10 mg. of deoxycortone acetate daily, but without clinical or biochemical improvement (see table). The renal function steadily deteriorated until on the 25th day the blood-urea level was 330 mg. per 100 ml. and the blood-uric-acid 17 mg. per 100 ml. The patient died in coma 31 days after admission.

Necropsy findings (Dr. D. H. Osborne).—The body was sparsely covered, with little subcutaneous fat. The heart was not enlarged, weighing 350 g. In the apices of both lungs were small areas of caseation surrounded by scar tissue, the remainder of both lungs being normal. The alimentary system was normal except for a suppurative swelling of the left parotid gland. The left kidney weighed 232 g., and several yellowish-white areas bulged through the capsule. On section a considerable amount of renal parenchyma was found to have become caseating masses, some of which communicated with the pelvis. The intervening tissue was mottled by more recent tuberculous lesions. The pelvis and ureter were moderately dilated and both were inflamed. The ureter was thickened and in its lower third would just admit a probe. The bladder showed slight congestion only, and the prostate and seminal vesicles showed evidence of tuberculosis. The adrenal glands were normal, and no abnormality was seen in the brain.

BIOCHEMICAL FINDINGS IN CASE 2

—	Aug. 3, 1951	Aug. 7, 1951	Aug. 23, 1951	Aug. 27, 1951
Serum-sodium (mg. per 100 ml.)	266 (*115*)	269 (*116*)	283 (*124*)	253 (*110*)
Serum-potassium (mg. per 100 ml.)	16 (*4·1*)	16 (*4·1*)	15·3 (*3·9*)	22·5 (*5·8*)
Serum-chloride (mg. per 100 ml.)	396 (*114*)	359 (*102*)	435 (*112*)	370 (*106*)
Plasma-bicarbonate (vols. per 100 ml.)	57·6 (*26*)	63·6 (*28·8*)	48·1 (*21·8*)	41·3 (*18·6*)
Blood-urea (mg. per 100 ml.)	147	150	126	330
Uric acid (mg. per 100 ml.)	..	..	..	17
Urine sp. gr.	1003	1004	1009	..
Urine sodium chloride content (mg. per 100 ml.)	..	272	212	..

Figures in parentheses represent m.eq. per litre.

Histological examination of the kidney showed widespread caseous tuberculosis (fig. 3) and in the areas not so affected changes that probably represent antecedent healed pyogenic pyelonephritis (fig. 4).

Case 3.—A boy, aged 18, was admitted in April, 1951, with a month's history of generalised cramps, weakness, and unsteadiness, and several months' history of mottled pigmentation of the face. There was no relevant family history, and he had worked as a farm labourer since the age of 14. He had always been very fit until the age of 16, when he had an attack of tonsillitis, followed by puffiness of the eyes and headaches. He first noted cramps soon after this illness. They were confined to his calves, and occurred after exercise and at night. He had always tanned easily in the summer, but the tan that he acquired in the summer of 1950 faded very slowly, leaving brown blotches on his face throughout the winter of

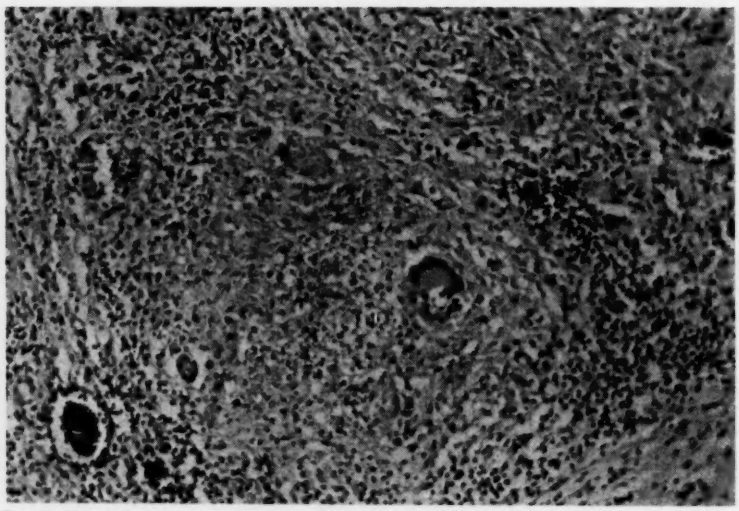


Fig. 3—Tuberculous granulation tissue, caseation, and interstitial inflammation (case 2). (Hæmatoxylin and eosin × 174.)

1950–51. In March, 1951, he noticed that he was rapidly becoming tired and breathless and had palpitations while doing the work to which he was accustomed. He also developed cramps of the hands and feet, and some shakiness. On one occasion he fainted. He was seen by his family doctor, who prescribed sodium chloride 16 g. daily by mouth, after which the cramps and unsteadiness were much improved, although he still felt weak and listless.

On examination patches of brown pigmentation were seen over his face and arms, but not on his buccal mucosa. Muscular twitching was noted during the examination. His blood-pressure was 140/65 mm. Hg, and his heart was not enlarged. All his reflexes were very brisk. His urine was of low specific gravity, seven specimens being below 1·010, and contained 2 g. of protein per litre. No formed elements were seen.

Treatment and progress.—It was thought that the diagnosis lay between Addison's disease and chronic nephritis, and the extra salt which had been prescribed was stopped for an observation period. He was given a normal diet, but with no added salt, and after 8 days the serum-sodium level had fallen to 302 mg. per 100 ml. (131 m.eq. per litre). On the 10th day he complained of weakness and nausea, and later began to vomit. His blood-pressure fell to 80/50 mm. Hg, but he rapidly improved when given salt by mouth. He continued to take sodium chloride 4 g. four times daily throughout his stay in hospital.

Investigations.—The blood-urea level was 205 mg. per 100 ml.; the blood-sugar 100 mg. per 100 ml.; the alkali reserve 26·2 vols. per 100 ml. (11·8 m.eq. per litre); the serum-calcium 8 mg. per 100 ml. (4 m.eq. per litre); the serum-phosphate 4 mg. per 100 ml. (1·25 m.eq. per litre); and the 17-ketosteroid excretion 7·95 mg. in 24 hours. After 10 days on 16 g. of salt daily, the serum-sodium level was 357 mg. per 100 ml. (156 m.eq. per litre) and the serum-chloride 367 mg. per 100 ml. (104 m.eq. per litre).

Discharge.—It was felt that the probable diagnosis was salt-losing nephritis, and that in view of the acidosis, and their response to salt, the cramps were due to the lack of sodium chloride rather than calcium. The patient was discharged, and recommended to continue to take 16 g. of salt daily.

Follow-up.—After his discharge he attended as an out-patient twice—in June, 1951, when he seemed in excellent health, and in January, 1952, when he said that he felt very well but had reduced his extra salt intake to 8 g. daily on advice from his doctor, who had noticed slight œdema of his ankles. He appeared much less pigmented than before, and his blood-pressure was 160/120 mm. Hg. The serum-sodium level was 350 mg. per 100 ml. (152 m.eq. per litre); the serum-chloride 340 mg. per 100 ml. (96 m.eq. per litre); the alkali reserve 42·4 vols. per 100 ml. (19·1 m.eq. per litre); the serum-potassium 19 mg. per 100 ml. (5 m.eq. per litre); and the blood-urea 110 mg. per 100 ml. The urine, sp. gr. 1·010, contained protein.

Readmission.—The patient was readmitted on March 16, 1952, having felt quite well until the end of February, 1952, when he noticed that his legs had become swollen up to the thighs: 2 days before admission he had developed a headache and vomiting.

On examination no cutaneous pigmentation was now visible. The blood-pressure was 180/130 mm. Hg, and a presystolic triple rhythm was audible in the heart. There was œdema of both ankles, and a small sacral pad, but the neck veins were not raised, and there was no pulmonary congestion. All the tendon-reflexes were very brisk, and Chvostek's sign was elicited. The urine, sp. gr. 1·010, contained protein 4 g. per litre and numerous granular casts. The serum-sodium level was 325 mg. per 100 ml. (142 m.eq. per litre); the serum-chloride 340 mg. per 100 ml. (96 m.eq. per litre); the alkali reserve 33·8 vols. per 100 ml. (15·7 m.eq. per litre); the blood-urea 150 mg. per 100 ml.; the serum-calcium 4·4 mg. per 100 ml. (2·2 m.eq. per litre); the serum-phosphate 4·26 mg. per 100 ml. (1·33 m.eq. per litre); the serum-potassium 17·1 mg. per 100 ml. (4·4 m.eq. per litre); the serum-creatinine 14·4 mg. per 100 ml.; the serum-alkaline-phosphatase 8·1 King-Armstrong units, and the serum-protein 6·15 g. per 100 ml. (14·9 m.eq. per litre).

Progress.—The patient rapidly developed generalised œdema, and on the

Fig. 4—Another part of the same kidney as in fig. 3, but distant from the tuberculous lesion; showing glomerular hypertrophy and sclerosis, interstitial scarring and inflammation, and tubular dilatation and hypertrophy, probably due to antecedent pyogenic pyelonephritis (hæmatoxylin and eosin × 104.)

18th day (April 3) began to vomit. Over the next 2 weeks this persisted, and he developed gross muscular twitchings and weakness. On the 32nd day (April 17) a pericardial friction rub was heard, and he died in uræmic coma on April 19, 34 days after admission.

Necropsy findings (Dr. J. B. Enticknap).—The adrenals were enlarged (20 g. each). Both kidneys were small, the left weighing 7·8 g. and the right 25 g. The left renal pelvis was larger than the kidney, and both ureters were dilated to a diameter of 1·2 cm. (fig. 5). The right kidney was about four times as big as the left, but was still markedly reduced in size, and showed gross scarring of the surface. Perinephric adhesions were present on both sides, and section showed the cortex to be narrowed to about 2 mm. Histologically there were present changes typical of chronic pyelonephritis. The heart was enlarged (460 g.), and there was a recent fibrinous pericarditis. There was hæmorrhagic ulceration throughout the gut. The parathyroid glands and all other organs were normal.

Fig. 5—Bilateral contraction of kidneys, left being much more affected than right and associated with dilatation and hypertrophy of pelvis and ureter (case 3).

DISCUSSION

Clinical Features

The six cases of salt-losing nephritis that have been previously reported comprise a clearly defined clinical group. The patients are usually young adults and, except for Thorn's patients, who experienced polyuria, have no history of renal disease or any symptom suggesting renal insufficiency. The illness presents with any or all of the symptoms of Addison's disease, including tiredness, weakness, anorexia, nausea and vomiting, cramps, collapse, and coma. All six of the reported cases and two of the three presented here (cases 1 and 3) were at one time diagnosed as adrenocortical failure, and this diagnosis was seriously considered in our other patient (case 2). In one patient carcinoma of the stomach was entertained as a possible diagnosis (Nussbaum et al. 1952).

Pigmentation of the skin, which has now been seen in three patients (Sawyer and Solez 1949, and the present cases 1 and 3), and the almost invariable absence of casts and cells from the urine make the diagnosis even more difficult. Some cases may be recognised by their failure to respond to deoxycortone acetate and adrenocortical extract or by the unusual degree of nitrogen retention and acidosis that exists. The diagnosis, if correct, can easily be confirmed by renal-function tests, which show gross impairment. Conversely, adrenocortical function, as shown by carbohydrate metabolism, 17-ketosteroid excretion, and response to adrenocorticotropic hormone (e.g., Thorn's test), will be found to be normal; whereas, tests of adrenal function that depend on intact renal tubules (e.g., the Kepler-Power test) are invalid in this condition.

Treatment by replacement of the lost sodium and chloride by doses of up to 20 g. of salt daily has enabled some patients to spend the rest of their lives in fair health. The longest recorded survival period has been $4^1/_2$ years (Thorn et al. 1944). Correction of acidosis by sodium bicarbonate (15 g. per day) has been tried by Sawyer and Solez (1949), but Nussbaum et al. (1952), who used sodium acetate, observed that a restoration of the alkali reserve of their patient was associated with clinical deterioration and subsequent death.

The two common causes of death seem to be collapse in a state of salt depletion (de la Balze and Oñátivia 1947, and the present cases 1 and 2) and hypertensive heart-failure with uræmia (Thorn et al. 1944, and the present case 3), a fate which seems to await those in whom the salt loss has been successfully treated. In addition, these patients, like all nephritics, are ill equipped to overcome the other hazards of existence. One is reported to have died after a surgical operation (Sawyer and Solez 1949); another suddenly, possibly as the result of retention of potassium (Nussbaum et al. 1952); and a third from pulmonary tuberculosis (Borst 1950), a disease which two of our three patients had (cases 1 and 2). It is recognised indeed that in case 2 the picture of renal salt loss was complicated by the concomitant tuberculosis, which, for example, led to the appearance of pus cells and considerable amounts of protein in the urine. Further, it is arguable that the illness was in some degree due to active tuberculosis. These reservations are valid, but nevertheless we consider on clinical and biochemical grounds that sodium depletion was the most important feature of his illness.

Pathological Features

The biochemical findings in this type of nephritis are those of loss of salt and water together with nitrogen retention and acidosis. It is evident that these patients must all be in negative sodium, chloride, and water balance, although these crucial observations have never been recorded.

Kidneys.—Necropsy findings have been reported in five previous cases. Chronic glomerulonephritis was seen in three (Thorn et al. 1944, Sawyer and Solez 1949); polycystic disease, with apparent specific tubular damage, in one (Borst 1950); and pyelonephritis in another (Nussbaum et al. 1952). Two of the present cases showed chronic pyelonephritis (fig. 1), and one tuberculosis and chronic pyelonephritis (figs. 3 and 4). In case 1 (fig. 2) calcification of the tubules was seen, a finding previously reported by Thorn et al. (1944) and Sawyer and Solez (1949). The functional impairment is of the whole kidney, but the special features of this condition suggest that the tubules are specifically damaged. This is to some extent supported by the anatomical observations already cited, and further by the observations that the tubules do not respond to deoxycortone acetate, parathyroid, or pituitary extract (Thorn et al. 1944, Borst 1950), or to cortisone (Nussbaum et al. 1952), and that renal secretion of ammonia is decreased (Thorn et al. 1944).

Serum changes.—Thorn et al. (1944) graphically demonstrated that the abnormality of serum-electrolytes is due to failure not of production of adrenal cortical hormone but of tubular response. This principle of "target organ" failure has recently been recognised in other conditions—e.g., pseudohypoparathyroidism (Albright et al. 1942). The derangement of renal function underlying nitrogen retention is better understood (Fishberg 1939) than are those which cause acidosis and loss of salt and water. Platt (1951), however, has shown that in most cases of chronic renal failure sodium balance is still maintained, and that, because glomerular filtration of sodium is diminished, this must imply a decrease in reabsorption of sodium by the tubules. In a few patients (Platt 1950) sodium loss was noted, and these may be regarded as potential salt-losing nephritics. Attention may also be drawn to the work of Pitts and Alexander (1945), who showed that the cells of the renal tubules can exchange hydrogen ions for sodium ions from the glomerular filtrate, and thereby eliminate acid and conserve base. Should this mechanism fail, acidosis together with excessive loss of salt and water would result, a condition similar to that seen in "salt-losing nephritis." Bull et al. (1950) have observed electrolyte loss in the recovery phase after prolonged anuria, when the tubules are specifically damaged, but this is a further acute episode in the course of a dramatic renal illness, and clinically distinct from "salt-losing nephritis." In this connection it may be noted that case 2 had two short

periods of anuria (6 hours and 24 hours). His blood-pressure was not, however, very low during either episode, and we do not feel that they were causally related to his salt loss.

If the state of acidosis were of sufficient duration, sources of base other than sodium would have to be found. Albright and Reifenstein (1948), basing their calculations upon results obtained by Shohl (1939), conclude that 49% of the calcium in the skeleton is available as a source of base. This might eventually be drawn on and, should the drain be excessive, the picture of renal osteodystrophy result. This point has been fully discussed by Snapper (1949), but it is interesting to note that in case 3 the serum-calcium level was reduced to 4·4 mg. per 100 ml. (2·2 m.eq. per litre), and that the skull in case 1 resembled that seen in Paget's disease, being thickened and soft, a finding common in renal osteodystrophy. A further point of resemblance is the metastatic calcification noted by Sawyer and Solez (1949). Excessive excretion of calcium might explain the calcification which these workers found in the glomeruli and tubules. Tubular calcification was seen in case 1 (fig. 2).

Pathological pigmentation of the addisonian type has once previously been recorded in this condition (Sawyer and Solez 1949). In the present case 1 it was classical, involving the buccal mucosa, pressure points, and normally pigmented areas. In case 3 it was not characteristically addisonian, but the brown blotches on the face were very striking when the patient was first seen in 1951. This finding too is common in renal osteodystrophy (Maddox 1932). No explanation is offered for the occurrence of addisonian pigmentation in salt-losing nephritis, but it seems unlikely that adrenal medullary failure plays a part in its production.

SUMMARY

Three new cases of salt-losing nephritis, with necropsy findings, are reported.

The previously recorded cases are briefly reviewed.

The clinical features of the condition are summarised. Two further cases showing pathological pigmentation of the skin are recorded.

The pathology of the condition is discussed.

Certain points of resemblance to renal osteodystrophy are noted.

We wish to thank Mr. W. D. Doherty and Dr. K. S. MacLean under whose care cases 2 and 3 were admitted; Dr. J. B. Enticknap for the histological reports and photomicrographs in all three cases and for the necropsy report in case 3; and Dr. J. C. Houston for helpful criticism and advice.

REFERENCES

Albright, F., Burnett, C. H., Smith, P. H., Parson, W. (1942) *Endocrinology*, **30**, 922.

— Reifenstein, E. C. jun. (1948) The Parathyroid Glands and Metabolic Bone Disease. London; p. 242.

Borst, J. R. (1950) *Acta med. scand.* **136**, 1.

Bull, G. M., Joekes, A. M., Lowe, K. G. (1950) *Clin. Sci.* **9**, 379.

de la Balze, F. A., Oñativia, A. (1947) *Medicina, B. Aires*, **7**, 60.

Fishberg, A. M. (1939) Hypertension and Nephritis. 4th ed., Philadelphia; p. 49.

Lancet (1952) i, 912.

Maddox, K. (1932) *Med. J. Aust.* i, 487.

Marriott, H. L. (1947) *Brit. med. J.* i, 245, 285, 328.

McCance, R. A. (1936) *Lancet*, i, 823.

Nussbaum, H. E., Bernhard, W. G., Mattia, V. D. jun. (1952) *New Engl. J. Med.* **246**, 289.

Peters, J. P., Wakeman, A. M., Lee, C. (1929) *J. clin. Invest.* **6**, 551.

Pitts, R. F., Alexander, R. S. (1945) *Amer. J. Physiol.* **144**, 239.

Platt, R. (1950) *Clin. Sci.* **9**, 367.

— (1951) *Lancet*, i, 1239.

Ravreby, L., Sawyer, W. H. (1948) *New Engl. J. Med.* **239**, 110.

Rosenheim, M. L. (1951) *Lancet*, ii, 505.

Sawyer, W. H., Solez, C. (1949) *New Engl. J. Med.* **240**, 210.

Shohl, A. T. (1939) Mineral Metabolism. New York; p. 31.

Snapper, I. (1949) Medical Clinics on Bone Diseases. 2nd ed., London; p. 97.

Soloff, L. A., Zatuchni, J. (1949) *J. Amer. med. Ass.* **139**, 1136.

Thorn, G. W., Koepf, G. F., Clinton, M. jun. (1944) *New Engl. J. Med.* **231**, 76.

Winkler, A. W., Crankshaw, O. F. (1938) *J. clin. Invest.* **17**, 1.

THE CONDITION OF THE KIDNEYS IN SALT-LOSING NEPHRITIS

J. B. ENTICKNAP
M.D., D.C.P.

From the Department of Pathology, Guy's Hospital, London

Thorn et al. (1944) reported 2 cases of a clinical syndrome which closely resembled Addison's disease and in which pathological changes were found only in the kidneys, the adrenal glands being normal. Several similar cases have since been reported by other workers (table I). The condition has recently been reviewed by Joiner and Thorne (1952a), who present 3 further cases seen at Guy's Hospital. Specimens from these patients were much alike, a fact which prompted a review of the pathological features of all the 8 cases hitherto reported.

MATERIAL AND METHODS

The published reports of the first 5 cases have been extracted and summarised, wherever possible in the author's own words. In 4 of these 5 cases the descriptions are full and detailed, but none of the reports includes a photomicrograph. For case 6 the original necropsy report was available together with paraffin blocks of one kidney, one adrenal gland, and a piece of skull. The necropsies in cases 7 and 8 were personally observed, and the relevant material was examined histologically by conventional methods.

RESULTS

These are summarised in the accompanying tables, and the last 3 cases have been illustrated by Joiner and Thorne (1952a). All the kidneys were affected by generalised disease, but in case 7, who had had a unilateral nephrectomy, much of the remaining kidney was destroyed by tuberculous pyelonephritis. The description of this organ both in the text and in the table is mainly concerned with the parts of it apparently unaffected by this process, in which it was thought that changes were present that had probably antedated the tuberculosis. Even if they did not they so closely resembled those due to pyogenic infection that the main argument is unaffected. While it is impossible to dogmatise on the lesions present in the first 5 cases, the published reports show that they are very similar to those found in the last 3.

Macroscopically (table I) these diverse kidneys had several common features. Ten of the twelve kidneys in which it was possible to make an estimate were contracted, and the presence of multiple cysts in the remaining two makes it unlikely that the weights are a measure of the amount of functioning renal tissue. In 5 of these 6 cases the contraction was bilaterally asymmetrical. Capsular adherence was common, the normal pattern was usually destroyed, and in all the cases but one the thickness of the cortex was reduced to less than 3 mm. The surfaces of the kidneys were granular, and cysts were seen in several cases. Some abnormality was present in the pelvis in all the 7 cases in which it was described.

Microscopically (table II) there were again numerous features in common. Reticular or radial scarring is specifically mentioned in 5 cases, in 2 no relevant comment is made, and in the remaining case the kidney was grossly distorted by the presence of multiple cysts.

The *interstitial tissue* in all the cases showed various amounts of fibrosis and was infiltrated by cells denoting chronic inflammation.

The *glomeruli* were variably affected in the different kidneys, but in none were the changes of active glomerular nephritis seen, and all the descriptions suggest or emphasise the fact that the changes were not evenly distributed. Capsular thickening was present in all the cases, but in only 1 were adhesions to the tufts described.

The *tubules* showed changes in all the cases. Some dilatation was present in them all, and the descriptions of the other features of the first 5, although varying in detail, were compatible with the presence of the lesion that was seen in the last 3: focal hypertrophy producing an epithelium of variable depth in dilated subcapsular tubules that alternated with scarred areas in which the tubules were atrophied. The so-called colloid casts were present in 5 cases, and hyaline and granular material in another. Pus cells were present in the tubules in 4 cases, but 1 of these was the case with renal tuberculosis. Calcification of the tubular basement membrane was seen in 3 cases, and focal glomerular calcification in 2.

Other Findings.—In 2 of the cases there was hypertrophy of the parathyroid glands, but in only 1 of these and in 1 other in which they were normal was there any osteomalacia. There was also a tendency to hypertrophy of the adrenal glands, the weights in the 3 patients for whom they are recorded being above the normal mean, and hyperplasia being described in another case.

Diagnosis.—In 4 of the 7 cases in which a definite pathological diagnosis was made the condition was said to be pyelonephritis.

DISCUSSION

These findings suggest that chronic pyelonephritis is the condition commonly responsible for this syndrome; so it becomes important to define this term. As used here it is almost synonymous with the chronic interstitial nephritis of the older descriptions, a term which might well be applied to all the kidneys referred to. Its main feature is the presence of a chronic inflammatory exudate in the interstitial tissue causing renal contraction that is commonly greater on one side than the other. Microscopically a reticular type of fibrosis (Russell 1929) is seen, and the most typical lesion is a radial band extending from the pelvic region to a coarse depressed stellate scar on the surface. Parenchymal lesions are mainly confined to these bands of scar tissue, in which tubular atrophy and glomerular hyalinisation together with arteriolar sclerosis and hyalinisation are commonly found. In between these scars tubular hypertrophy and dilatation are present, and in many cases this proceeds to the stage of formation of small cysts in which the so-called colloid casts may be seen. Eventually numerous large cysts may develop, a condition much more commonly due to interstitial fibrosis than to the parenchymal inflammation of a predominantly glomerular nephritis (Weiss and Parker 1939). Numerous smaller points of differentiation have been described but are not sufficiently exclusive to be of real diagnostic value.

I have discussed elsewhere (Enticknap and Joiner 1952) whether the term "chronic pyelonephritis" is the best name for the condition present in kidneys showing these appearances, and have provisionally concluded that it is. In such cases that present, as these subjects did, with some form of renal failure, the disease has probably developed from repeated minor attacks of hæmatogenous renal infection following asymptomatic transient bacteræmias. It is becoming increasingly recognised (see Enticknap and Joiner 1952 for references) that this condition is perhaps the commonest single form of Bright's disease; hence it is not surprising that several of the cases in the present series were so diagnosed and that they were the ones more recently published. The first 4 cases may therefore be re-examined to see whether they too are not examples of a similar condition. Cases 1 and 4 and cases 2 and 3 will be discussed together because they present similar appearances.

Cases 2 and 3 both have much contracted kidneys from which nearly all pathognomonic changes have disappeared, and it is perhaps unwise to attempt to diagnose them too precisely solely from the condition of the kidneys. Clinically case 2 had only a trace of protein in the urine, whereas case 3 had none, and in neither case were casts found, findings quite unlike those of the terminal stages of chronic glomerular nephritis. A further point is that case 2 had hypertrophy of one parathyroid gland and softening of the ribs. Gilmour (1947) showed that secondary hyperparathyroidism in acquired renal

TABLE I—MACROSCOPIC APPEARANCES OF KIDNEYS

Case no.	Reference	Original author's diagnosis	Kidney weights (g.)		Capsule	Surface	Normal pattern	Pelvis
			R	L				
1	*Thorn et al. (1944)*: Case 1	None given	140	140	Adherent	Finely granular and showing numerous cysts	Destroyed by cysts, cortex reduced to a few mm.	A few submucosal hæmorrhages
2	Case 2	Diffuse glomerulonephritis in the final state	60	42	Adherent and thickened	Finely granular with a few cysts	Destroyed, a few cysts present, cortex 1·0–2·5 mm. thick	A few hæmorrhages and some increase in fat
3	*Sawyer and Solez (1949)*	Severe chronic glomerulonephritis	70	70	Adherent	Finely granular	Poorly demarcated, cortex 3 mm. thick	Submucosal hæmorrhages
4	*Borst (1950)*	Bilateral cystic disease	Combined weight 770		..	..	Innumerable cysts, from pinhead size to 3 mm. in diameter	..
5	*Nussbaum et al. (1952)*	Acute superimposed on chronic pyelonephritis	80	110	Adherent	A few cysts	Cortex of normal thickness	Purulent exudate
6	*Joiner and Thorne (1952a)*: Case 1	Chronic pyelonephritis	18	31	Stripped fairly readily	Granular with depressed scars	Not present	Small papilloma
7	Case 2	Tuberculous pyelonephritis	..	232	..	Mottled with yellow areas	Distorted by tuberculosis	Slightly dilated, ureter thickened
8	Case 3	Chronic pyelonephritis	25	8	Adherent to kidney and perinephric tissue	Coarsely granular with depressed scars and a few cysts	Destroyed, a few small cysts present, cortex 1–2 mm. thick	Dilated to twice the normal size on side of smaller kidney; a few hæmorrhages

disease was found almost exclusively in chronic pyelonephritis, a finding which agrees with experience in this hospital (Joiner and Thorne 1952b). Finally it may be pointed out that the label "glomerulonephritis" attached to these cases by the original American workers does not necessarily preclude their being examples of chronic pyelonephritis as defined, for it may merely reflect the absence of agreement on the significance of the terms used in renal pathology. It is therefore concluded that these 2 cases are examples of contracted kidneys in the sense that the term has been used elsewhere (Enticknap and Joiner 1952); and, although the question of their origin must be left undecided, it was found in the investigation referred to that such kidneys occurred most commonly in patients thought clinically to have chronic pyelonephritis.

Both cases 1 and 4 had kidneys containing multiple cysts and accordingly of normal or increased weight. In case 1, not diagnosed by Thorn et al. (1944), there can be little doubt from the description that the condition was inflammatory and almost certainly due to chronic pyelonephritis. Much parathyroid hyperplasia was again present. The weight of the kidneys in case 4 makes this diagnosis much less likely, but the description given is fragmentary. Probably the correct diagnosis is congenital polycystic disease, but the fact that this patient was not hypertensive makes this uncertain. In any event such kidneys commonly show evidence of superadded infection, fibrous replacement of renal parenchyma following repeated attacks being the probable morphological basis of ultimate renal failure, and much proliferation of interstitial connective tissue is emphasised in the description. Case 1 is then almost certainly one of chronic pyelonephritis, and case 4, although probably having some other renal abnormality as well, shows changes that strongly suggest the presence of the same condition.

TABLE III—OTHER FINDINGS

Case no.	Parathyroid glands	Bones	Adrenal glands	Other necropsy findings	Urine
1	5·7 g.	Normal	16·5 g. and 24 g.	..	No proteinuria and no casts
2	1 of the 3 found was larger than normal	Ribs soft	7·5 g. and 8·8 g.	..	Trace of protein and no casts
3	Normal	Normal	Hyperplasia	..	No protein and no casts
4	..	..	Normal	Hilar node, pulmonary and miliary tuberculosis	..
5	..	..	Normal	..	..
6	..	Skull soft but histologically normal	Normal	..	..
7	Normal	Normal	Normal	Previous unilateral nephrectomy for tuberculosis	..
8	Parenchyma weight 105 mg.	Normal	Large, about 20 g. each	..	..

Extensive tubular changes, giving rise in most cases to cyst formation, are a uniform feature of the histology of these kidneys. This is of interest in view of the conclusion of Joiner and Thorne (1952b) that the tubules are the site of the biochemical abnormality.

In summary it may therefore be said that 4 of these

TABLE II—MICROSCOPIC APPEARANCES OF KIDNEYS

Case no.	General appearance	Interstitial tissue	Glomeruli	Glomerular capsules	Tubules	Casts and tubular contents	Calcification of tubules
1	Extensive scarring widely separating cystic tubules and atrophied glomeruli	Hyaline fibrosis with plasma cells, mononuclears, and lymphocytes	Mostly hyalinised; preservation of single tufts in a few only	Pericapsular fibrosis	Dilated; flattened epithelium	"Colloid" casts	Present
2	..	Numerous lymphocytes	Mostly hyalinised; remainder hypertrophied; a few capillary thrombi	Adenomatous proliferation of epithelium; a few hyaline crescents	Dilated and hyalinised proximal tubules	Hyaline, granular, pus-cell, and "colloid" casts	..
3	..	Increased connective tissue; round cells	Reduced in number; mostly hyalinised, some lobulation and calcification	Thickened and adherent to tufts	Patchy distribution of atrophy and hypertrophy	None	Present
4	Multiple cysts	Much proliferation of connective tissue	Those present are intact	..	Severe degenerative changes, especially inconvoluted tubules; 2nd c.t. dilated	2nd c.t. contain hyaline and granular material	..
5	Patchy scarring	Increased fibrous tissue, with lymphocytes and plasma cells	Some degeneration	Thickened	Hypertrophy and dilatation	"Colloid" casts and pus	..
6	Reticular fibrosis with changes most marked in the radial scars	Gross fibrosis and some pus cells	Some hypertrophied and others with focal capillary hyalinisation and calcification	Some pericapsular fibrosis	Atrophy dilatation and hypertrophy; a few cysts 1–4 mm. in diameter	"Colloid" casts and some pus cells	Present
7	Radial areas of tuberculosis; radial scarring	Fibrosis and round-cell infiltration	Hyalinisation in radial scars only	Some fibrosis	Dilated and hypertrophied between scars in subcapsular region; destroyed elsewhere	Pus cells	..
8	Reticular scarring and gross distortion	Increased fibrous tissue and lymphocytes	Mostly hyalinised A few grossly contracted glomeruli within dilated capsules showing plicated endothelium	Thickened	Atrophy, dilatation, and hypertrophy	"Colloid" casts	..

cases had chronic pyelonephritis in association with the salt-losing syndrome. In 2 further cases there was present in addition another serious renal condition, tuberculous pyelonephritis in one, and a form of cystic disease in another. In the remaining 2 patients inflammatory fibrosis had caused such gross distortion of the kidneys that it was impossible to be certain of the initial condition, which may well, however, have been pyelonephritis. In view of these findings it may be questioned whether salt-losing *nephritis* is the best possible name for this very important syndrome, and I suggest that, until the biochemical abnormality responsible is elucidated, it is better to use a circumlocution such as "urinary salt loss due to renal disease" or, perhaps much more neatly, "Thorn's syndrome."

SUMMARY

The renal findings in the 8 published cases of the salt-losing nephritis syndrome of Thorn et al. (1944) are described.

Chronic pyelonephritis was certainly present in 4 of them, probably present in 6 of them, and may well have been present in all 8 cases.

Since this condition is the only common pathological feature of these cases, the syndrome is probably an unusual response to it and the term "salt-losing *nephritis*" is not an accurate description.

REFERENCES

Borst, J. R. (1950) *Acta med. scand.* **136**, 1.
Enticknap, J. B., Joiner, C. L. (1952) Unpublished.
Gilmour, J. R. (1947) The Parathyroid Glands and Skeleton in Renal Disease. London.
Joiner, C. L., Thorne, M. G. (1952a) *Lancet*, ii, 454.
— — (1952b) *Guy's Hosp. Rep.* **101** (in the press).
Nussbaum, H. E., Bernhard, W. G., Mattia, V. D. jun. (1952) *New Engl. J. Med.* **246**, 289.
Russell, D. S. (1949) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 142.
Sawyer, W. H., Solez, C. (1949) *New Engl. J. Med.* **240**, 210.
Thorn, G. W., Koepf, G. F., Clinton, M. jun. (1944) *Ibid*, **231**, 76.
Weiss, S., Parker, F. jun. (1939) *Medicine, Baltimore*, **18**, 221.

RETARDATION OF GROWTH ASSOCIATED WITH HIRSCHSPRUNG'S DISEASE

F. A. R. STAMMERS
C.B.E., T.D., Ch.M. Birm., F.R.C.S.
PROFESSOR OF SURGERY

A. J. H. RAINS
M.B. Lond., F.R.C.S.
LECTURER IN SURGERY

UNIVERSITY OF BIRMINGHAM

ALTHOUGH for the past thirty years neuromuscular dysplasia or incoördination has been accepted as the cause of congenital megacolon (Hirschsprung's disease), and has supplanted the theory of valves or kinking of the colon at the rectosigmoid junction as the result of fæcal loading, a better understanding of the pathogenesis of the condition has been given by the work of Bodian et al. (1949) and Swenson et al. (1949).

Sir Arthur Keith (1915) was aware that much could be learnt of the pathology of the colon by a study of the "Auerbach tissue," as he called the functioning complex of ganglia and nerves lying within the muscle of the gut. He investigated its anatomy and pathology when Arbuthnot Lane was doing colectomy for intestinal stasis, and the discovery of some abnormality in the neuromuscular complex was anticipated as corroborative evidence in support of such treatment. Keith did not claim that the genesis of stasis had been solved:

> "Although my investigations have not succeeded in finding a pathological basis for impaired mobility of the colon, they may be of service in another way, by drawing attention to our considerable ignorance concerning both the anatomy and physiology of the great bowel."

Surgical textbooks of the day—e.g., Miles (1923)—always pointed out that there were two types of megacolon: one in which dilatation and hypertrophy extended from the anus upwards, and another in which various lengths of the rectum appeared normal in every respect. It is in this second type that Bodian et al. (1949) have shown an abnormality of "Auerbach tissue" in the seemingly normal portion of the rectum—namely, absence of ganglion cells, with some increase in size of the nerve-fibres. Swenson et al. (1949) have also demonstrated this abnormality and confirmed it by the manometric recordings of peristalsis. However, they do not suggest that there is absence of ganglion cells in all cases of congenital megacolon. Until this work, attention had always been focused on the dilated and hypertrophied portion of colon.

In view of these recent observations it has been suggested that the term congenital megacolon should be restricted to the second of the above-mentioned types, which usually manifests itself shortly after birth, the other types of megacolon with achalasia of the anal sphincter being excluded (Stephens 1951). Although this conception is based upon the time of onset of the disease in the life of the patient, together with the histological findings, it is really necessary to have proof of absence of some structure or of some function of the anal canal before such a distinction can be made permanently. Congenital weakness or imbalance may not show itself in the first few years.

The life history of these unfortunate victims who are deprived of the means of normal rectal and colonic evacuation is chequered with constipation and crises of such a degree of fæcal retention and impaction that, besides the effect of toxin absorption, peritonitis and death may result from perforation of stercoral ulceration. The least discomfort that the patient can have to endure is a rectal washout every week or so, and periodic manual evacuation of the rectum superimposed upon the obstinate constipation. If the lesion is more than a few inches from the anal canal, such conservative measures as rectal dilators and rectal washouts have little or no chance of permanent success compared with those cases of achalasia of the anal sphincter which Hurst (1924) declared could be treated in this way. Spinal anæsthesia (Telford and Simmins 1939) may be effective if given early enough in the life of the child, but a permanent result cannot be expected where "Auerbach tissue" is absent.

What is the quality of the life of one who suffers from this absence of "Auerbach tissue" and what is its duration? The quality is poor, being probably due to the absorption of toxins from the colon, for the general health is not good and the body is thinly covered and undernourished. The duration may be as short as a few weeks; but, even if early crises are survived, death may come from perforation or from intercurrent infection in adolescence. Adult life is rarely attained. Published reports give little or no information about the effect on physical and mental development or on endocrine balance that the condition may have if the patient survives; and no worker has reported such a remarkable delay in development, followed by an even more remarkable transformation after colectomy, as in the case described here.

CASE-RECORD

The patient was born in 1931. At the age of 11 days he was admitted to hospital with vomiting and signs of intestinal obstruction, and this early crisis was overcome with conservative measures. For the next 3 years the boy was in and out of various hospitals with attacks of obstruction. At the age of 3 years he was brought to the Children's Hospital, Birmingham, and there diagnosed as a case of Hirschsprung's disease. Admission was advised, but while he was on the waiting-list he had a further attack of obstruction. This time the distension and colonic impaction of fæces were so severe that a hard core of fæces was protruding through the anus. One of us (F. A. R. S.) did a cæcostomy and manual evacuation of the rectum as an emergency device to afford relief. Later on in his 3rd year the boy underwent presacral

sympathectomy and section of the lumbar colonic nerve; but no permanent relief was obtained, and his abdomen remained grossly distended. Yet there was some improvement, and because of this, and because of the war, he was lost sight of until he was aged 18, when he was admitted to Queen Elizabeth Hospital, Birmingham, for further investigation and treatment because he never had a spontaneous bowel action, fæcal impaction being prevented by enemata every other day. He had found that he could sometimes pass flatus if he lay steeply inclined with the pelvis high, so that the sigmoid could straighten out by gravity. He sought advice because his abdominal distension caused increasing breathlessness on exertion.

On examination he was very small, like a child aged 10 years rather than 18; his voice had not broken, his genitalia were undeveloped, and he had no pubic or axillary hair. His abdomen was enormously distended (fig. 1), and peristaltic waves were visible, often preceded by pain sufficient to make him cry out.

Fig. 1—Enormous distension of abdomen, tiny chest, and flaring of ribs.

Investigations.—The blood-pressure was 100/60 mm. Hg. Blood-count: hæmoglobin 36%, red cells 3,500,000 per c.mm.—a severe microcytic hypochromic anæmia.

Radiography of the chest was normal. The report on the abdomen was: "One can only call the fæcal accumulation fabulous." The report on the epiphyses was: "The bones are slender with wide marrow cavities. The union of the epiphyses to the shafts is a little delayed. That for the radial head should have fused at puberty; that at the distal end of the humerus should just be fusing."

Progress.—Even while enemata were being given to remove the accumulation of fæces the patient developed obstruction with vomiting and increase in the distension, but the crisis was overcome by further washings, and during the following fortnight enormous stools were obtained. The abdomen became much softer, but the large hypertrophied colon could easily be felt. It was decided to do a laparotomy to see if anything, possibly a colectomy, could be done to help the patient.

Operation (F. A. R. S.).—On July 18, 1949, the abdomen was opened through a left paramedian incision. Gross hypertrophy and dilatation of the ascending, transverse, descending, and sigmoid colon were found. The mesocolon and mesosigmoid were enormously thickened. The cæcum was normal. At the rectosigmoid junction the bowel suddenly narrowed, and the lumen appeared constricted for half an inch, at which point there seemed to be an increase in the circular muscle-fibres; distal to this point the bowel was narrow (fig. 2). It was decided that a colectomy was contra-indicated by the patient's poor condition and by his patulous anal sphincter, which would probably leave him incontinent after a colectomy with anastomosis of the ileum to the rectal stump. It was suggested that a plastic procedure like that used in Heller's operation for cardiospasm or in the Fredet-Rammstedt operation for pyloric stenosis in infancy could be tried. This plastic procedure at the site of constriction was undertaken, and longitudinal and circular muscle-fibres were divided vertically for three inches, and the incision was deepened until the mucosa began to pout through the incision. The rectum was not opened, but the bared area with pouting mucosa was covered by overlapping the appendices epiploicæ from each side; a pelvic drainage tube was inserted as a safety measure in case of leakage. The abdomen was closed.

Fig. 2—Thickened dilated sigmoid colon joining apparently normal rectum found at plastic operation.

Postoperatively the patient could pass flatus through the tube, and 4 days later he had a spontaneous bowel action. From then on he had several actions of good amount each day, and his general condition was much improved. He was delighted, because this was the first time in his life that he had ever had a spontaneous action.

On discharge his hæmoglobin had risen from 36 to 66%, his abdomen was considerably less distended, and he was learning abdominal exercises so that the muscles could regain their tone after being continually overstretched.

Relapse.—After 3 months of spontaneous bowel actions constipation recurred, and in 6 months the patient was admitted to another hospital as an emergency case with

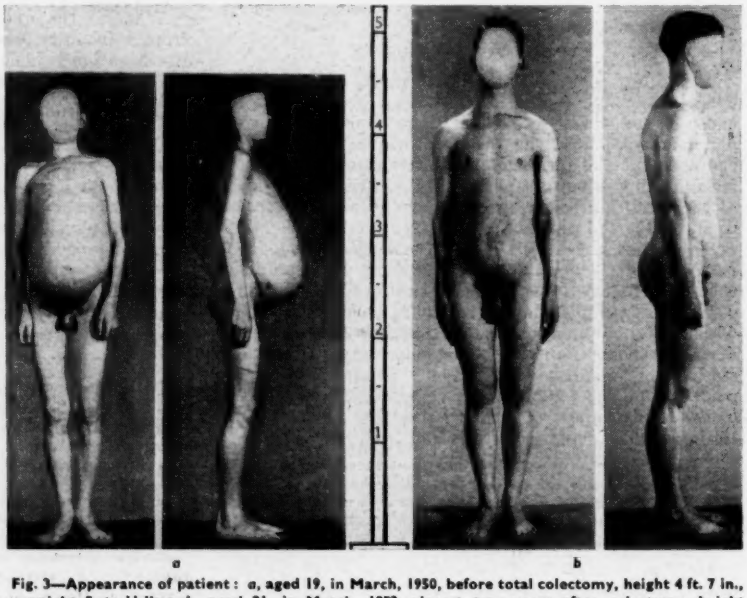


Fig. 3—Appearance of patient: *a*, aged 19, in March, 1950, before total colectomy, height 4 ft. 7 in., weight 5 st. 11 lb.; *b*, aged 21, in March, 1952, almost two years after colectomy, height 5 ft. 4 in., weight 8 st. 7 lb. Note recovery of stretched abdominal muscles in spite of operation scars.

obstruction of the large bowel. This obstruction was temporarily relieved by enemata, and after this he was admitted once more under one of us (F. A. R. S.). This time it was decided that total colectomy with anastomosis of the lower ileum well down on to the apparently normal rectum offered the only chance of success. The patient was now aged 19 and still looked as poorly nourished and infantile as before, and the distension of his abdomen was considerable (fig. 3*a*). His hæmoglobin was 46% and red cells 3,000,100 per c.mm. Repeated blood-transfusions were given before operation, raising the hæmoglobin to 86% and the number of red cells to 4,700,100 per c.mm. The serum-chloride and serum-protein levels were normal.

Total colectomy (F. A. R. S.).—On April 4, 1950, laparotomy was done through a midline incision, and the huge colon was found with many adhesions over the cæcum. The bowel at the rectosigmoid junction, where the previous plastic operation had been done, was found to be dilated, and below this the rectum appeared normal in size and on palpation. The site of the plastic operation was almost obliterated by scar tissue. Total colectomy was done (fig. 4). The distal ileum was anastomosed end-to-side with the rectum after the upper cut end of the latter had been closed by invagination.

Postoperatively the patient's general condition was good, but in the first 2 days he had severe abdominal colic, and it was noticed more than ever how child-like the patient was in his response to the pain and considerable discomfort. On the 3rd day he passed fæces and flatus; on the 4th and 5th day he had diarrhœa, having his bowels open five and seven times a day; on the 6th day his bowels were opened twice; and subsequently, although the motions were loose, he had no more than two or three actions daily until he was discharged on April 22, 1950.

Fig. 4—Colon removed at second operation. Note foot rule and size of appendix, which escaped dilatation and hypertrophy.

Pathological report on the apparently normal area below the dilated sigmoid: "Ganglion and nerve-fibres present in the position of Auerbach's and Meisner's plexuses. The muscularis of the colon below the stricture shows infiltration with lymphocytes and plasma cells."

Follow-up.—Two years have gone by since the colectomy; and in that time, besides maintaining spontaneous rectal evacuation from once to three times a day with no looseness or diarrhœa, the patient has been physically and mentally transformed. He is now aged 21, with a healthy agile mind and body (fig. 3*b*), looking forward to hard work and a good future. He is an engineering apprentice and in his spare time enjoys cycling and a great deal of ice skating. In April, 1952, he was 5 ft. 4 in. in height (4 ft. 7 in. before colectomy) and 8 st. 7 lb. in weight (5 st. 11 lb. before). The genitalia have developed, and all secondary sexual characteristics are present. His hæmoglobin is 92%, and radiography of the long bones shows (Dr. J. F. Brailsford) "evidence of some delay in ossification. The appearances suggest that the skeleton temporarily retarded has established its potential growth. The main epiphyses have now fused. There is no indication of giantism."

DISCUSSION

Diagnosis

The history of obstinate constipation from birth, with failure of spontaneous bowel action until the plastic operation at the age of 18, the crises of fæcal impaction, the failure of more conservative operations, together with the typical appearance shown by a fractional barium enema and the findings at operation (fig. 2), mark the patient as having congenital megacolon with dysplasia of the apparently "normal" segment of the rectum.

Rationale of Operation

For the extreme distension of fæcal impaction in a small child cæcostomy is a life-saving operation, overcoming obstruction and preventing perforation from stercoral ulceration; and the consequent improvement in the patient's condition makes it possible to empty the large bowel with less risk. There is no doubt of the good effect obtained in the present case.

Some operations become popular as the result of experimental work on a particular subject, and this was true in the early 'thirties of presacral neurectomy and section of the lumbar colonic nerve following the contributions of Learmonth and Markowitz (1930) and Rankin and Learmonth (1930) to the understanding of the autonomic system in the pelvis. Sympathectomy had just made its début, and reports of its application and results were beginning to come in (Stammers 1932). In the present case, however, there was no striking improvement. The plastic operation of 1949, done on the same lines as that for achalasia of the cardia or for congenital hypertrophic pyloric stenosis, was attended with some, though only temporary, success, for it was after this that the patient had the first spontaneous bowel action of his life. The cause of the failure may have been, just as it can be with rectosigmoidectomy, that the operation was not carried past the affected area of rectum. Had this been done, success might have lasted longer, though it must be observed that in the temporary period of 6 months of success there was no improvement in growth and development.

Total colectomy and not rectosigmoidectomy was done because the colon had been dilated and hypertrophied for 19 years and was involved right up to the cæcum; toxic absorption from the colon was causing delay in growth and development; and total colectomy in one stage for ulcerative colitis is not considered dangerous provided that the water and electrolytic balance of the patient is maintained. Colectomy for intestinal stasis on the grounds that it causes absorption of toxins was advocated and practised by Lane (1915) and Ward (1915).

The remarkable result that attended total colectomy in the present case supports the theory of toxic absorption (Mutch 1915), for some factor must have entered the body from the colon to retard growth and development to such an extent. One may wonder whether the same result would have been obtained by rectosigmoidectomy, by which operation the affected area of apparently normal rectum would have been excised but the proximal colon would have been retained. This may well be doubted, since no such change followed the plastic operation, although spontaneous bowel actions occurred.

Little is known of the toxins that can be absorbed from the bowel or be responsible for such a condition. Although such absorption is held to be the cause of a sallow skinned and poorly developed body with equivalent mental features, as is often seen in those who have prolonged obstinate constipation, this patient's mind and agility were of a high standard considering the stress imposed by the protuberant abdomen. Some other "toxin" must have been absorbed which had a direct effect on the pituitary gland.

In the last few years interest has been focused on necessary growth-promoting substances, such as vitamin B_{12}, and their association with bacterial activity and antibiotics. Perhaps in megacolon the absorption of these substances is prevented by the effects of stagnation in the dilated large bowel, effects which may even cause severe retardation of endocrine function. The more recent discovery of the rôle of pantothenic acid as an enzyme in the formation of acetylcholine may provide further impetus for research in Hirschsprung's disease. Although Swenson et al. (1949) have shown that the ganglion cells were absent in some of their cases, they state that this is not always so, this point being borne out in the case reported here. Perhaps an upset of the normal bacteriology of the colon, with incomplete

synthesis of pantothenic acid and the failure to absorb growth-promoting substances, may be responsible for much of the pathology of Hirschsprung's disease. Though this is conjecture it is an additional pointer to the fact that the pathology of Hirschsprung's disease is not yet completely known.

REFERENCES

Bodian, M., Stephens, F. D., Ward, B. C. H. (1949) *Lancet*, i, 6.
Hurst, A. F. (1924) Essays and Addresses on Digestive and Nervous Diseases and on Addison's Anæmia and Asthma. London.
Keith, A. (1915) *Brit. J. Surg.* **2**, 576.
Lane, W. A. (1915) *Ibid*, p. 599.
Learmonth, J. R., Markowitz, J. (1930) *Amer. J. Physiol.* **94**, 501.
Miles, A. (1923) *In* Choyce, C. C. System of Surgery. 2nd ed., London; p. 457.
Mutch, N. (1915) *Brit. J. Surg.* **2**, 608.
Rankin, F. W., Learmonth, J. R. (1930) *Ann. Surg.* **92**, 710.
Stammers, F. A. R. (1932) *Brit. J. Surg.* **20**, 67.
Stephens, F. D. (1951) British Surgical Practice Progress. London; p. 163.
Swenson, O., Rheinlander, H. F., Diamond, I. (1949) *New Engl. J. Med.* **241**, 551.
Telford, E. D., Simmins, H. T. (1939) *Brit. med. J.* ii, 1224.
Ward, L. E. B. (1915) *Brit. J. Surg.* **2**, 655.

TREATMENT OF THE ADRENOGENITAL SYNDROME WITH CORTISONE

DOUGLAS HUBBLE
M.D. Lond., M.R.C.P.

PHYSICIAN, DERBYSHIRE ROYAL INFIRMARY, DERBY CITY HOSPITAL, AND DERBYSHIRE HOSPITAL FOR SICK CHILDREN

THE manifestations of the adrenogenital syndrome in girls and women at or after puberty respectively are hirsuties, acne, enlargement of the clitoris, and amenorrhœa or irregular scanty menstruation. Although some of these patients may have a daily excretion of 17-ketosteroids within average limits (5–15 mg.), if the output of 17-ketosteroids is followed over a long period it can be shown in many instances to exceed 20 mg. daily. This increased excretion is intermittent and varies in amount; it has been reported by Koets (1949) to be greatest in the phase of ovulation, and by Merivale (1951) to be maximal in the luteal phase. The recognition that cortisone depressed adrenocortical function soon led to its use in conditions of adrenocortical excess. Wilkins et al. (1951, 1952) have described its use in eleven children for 5–17 months, and Bartter et al. (1951) have described the results of treatment in three patients. Bishop et al. (1952) and Simpson (1952) have reported its use for a short time in two patients with adrenocortical hyperplasia.

In the case reported here a girl, aged 19, with virilism, was studied for ten months, during the last five of which she was treated continuously with cortisone.

CASE-RECORD

The patient, who was referred to me from the dermatological department of the Derbyshire Royal Infirmary by Dr. P. D. C. Kinmont for investigation of hirsuties, complained of an excessive growth of hair on her face since the age of 15, more marked on the cheeks than on the lip and chin (see figure). She shaved three or four times a year. Her menses started at the age of 13 and were irregular during the first two years, with periods of amenorrhœa lasting three or four months. From the age of 15 to that of 17 the intervals between periods were about a month, but during the last year usually 31–33 days.

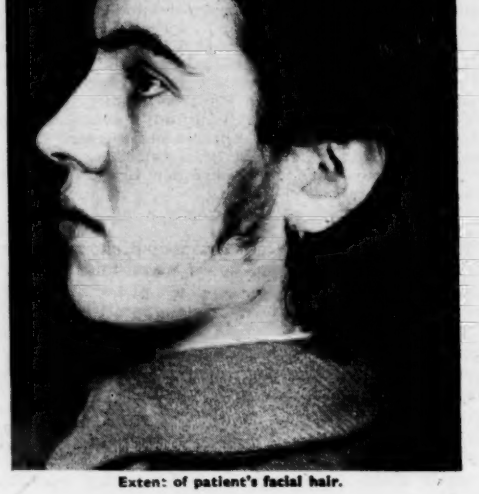
On examination the patient had a few hairs round the areolæ of the nipples and a male distribution of hair on the abdomen. The growth of hair on the back and on the legs was excessive. There was a moderate amount of acne on the face and back. The labia minora were reported by a gynæcologist (Mr. N. L. Edwards) to be hypertrophied, and the clitoris to be enlarged.

Investigations.—A tumour of the adrenal cortex was excluded, and the usual endocrine functions were investigated and found to be within average limits except in two aspects. The urinary excretion of 17-ketosteroids was intermittently greater than usual. In 25 estimations done in five months the average daily excretion was 15·2 mg. per twenty-four hours, the lowest figure being 7·0 mg. and the highest 33 mg. per twenty-four hours. It could not be determined that the rise or fall of 17-ketosteroids was related to definite intermenstrual phases, nor were the highest levels associated with the increase of pregnanediol in the luteal phase. The other abnormal finding was that on 6 out of 23 occasions the serum-potassium level was lower than normal; the lowest of these six readings was 12·2 mg. per 100 ml. (3·1 m.eq. per litre), and the average 14·5 mg. per 100 ml. (3·7 m.eq. per litre). On three of these occasions the serum-sodium level was above normal: 334, 340, and 344 mg. per 100 ml. (145, 147, and 149 m.eq. per litre). The plasma-chloride level, the alkali reserve, and the urinary output of sodium, potassium, and the chlorides were invariably within accepted average limits. The eosinophil-count was always between 200 and 500 per c.mm.

Treatment.—The patient was first given a week's treatment with 100 mg. of A.C.T.H. daily. This produced an eosinophil-count averaging 60 per c.mm. (ten counts), and an excretion of 17-ketosteroids averaging 24·0 mg. per twenty-four hours (six estimations). The day-time output of urine in the five days preceding A.C.T.H. therapy was 182 oz. (daily average 36·4 oz.) and the nocturnal output 93 oz. (nightly average 18·6 oz.). In the first four days of A.C.T.H. therapy the day-time output was 84 oz. (daily average 21 oz.) and the nocturnal output 144 oz. (nightly average 36 oz.). The daily average serum-potassium level in the first four days of A.C.T.H. therapy was 13·9 mg. per 100 ml. (3·6 m.eq. per litre). In the last two days of the week of A.C.T.H. therapy the serum-potassium level was normal and the ratio of diurnal to nocturnal urine was corrected. At the end of five weeks, and before cortisone therapy was started, the patient's cheeks were shaved and the hair removed was weighed. This was repeated at the end of four further five-week periods, during which the dose and method of administration of cortisone varied (see table).

RESULTS OF TREATMENT

These findings confirm the therapeutic results obtained by Wilkins et al. in adrenocortical hyperplasia in children. Cortisone will suppress the excessive androgenic activity of the adrenal cortex, and Wilkins et al. suggest that, to sustain an optimal therapeutic effect, the excretion of 17-ketosteroids should be kept less than 8 mg. per twenty-four hours. In the present patient with varying dosage this level was maintained for periods of no longer than two weeks, and a detailed examination of the records suggests that this level might be permanently



Extent of patient's facial hair.

RESULTS OF CORTISONE THERAPY

—	First 5 weeks	Second 5 weeks	Third 5 weeks	Fourth 5 weeks	Fifth 5 weeks
Average daily dosage of cortisone (mg.)	Nil	50 (1)	25 (2a & b)	40 (3a & b)	40 (4a, b & c)
Weight of hair removed (mg.)	99	50	70·8	68	58
Average daily excretion of 17-ketosteroids (mg.)	20	10·3	11·5	10·5	10·4

Method of administration :
1, 25 mg. by injection twice daily.
2(a) 2 weeks, 50 mg. orally (*i* = 25 mg. by injection).
(b) 3 weeks, 25 mg. by injection daily.
3(a) 1 week, 25 mg. by injection twice daily.
(b) 4 weeks, 50 mg. by injection on alternate days.
4(a) 2 weeks, 50 mg. by injection on alternate days.
(b) 2 weeks, 25 mg. twice daily.
(c) 1 week, 100 mg. on alternate days.

sustained with a daily injection of 50 mg. or an injection of 100 mg. on alternate days. The same dose by mouth was ineffective, and Wilkins et al. advise that, for an equal suppressive action, the oral route requires two or three times the amount given by injection.

It will be seen from the table that there is a rough correlation between the amount of hair growth, the dose of cortisone, and the amount of 17-ketosteroids excreted. It is shown that the rate of excessive hair growth can be about halved, but that it can be completely suppressed by cortisone therapy is as yet uncertain.

MODE OF ACTION

It is assumed that cortisone suppresses adrenocortical activity by opposing the action of A.C.T.H. Bartter et al. suggest that the androgenic excess may be due to a relative insufficiency of 11,17-oxysteroid production (which is the major opponent and regulator of A.C.T.H. secretion) with a consequent excessive secretion of A.C.T.H.

The present patient showed no evidence of 11,17-oxysteroid insufficiency (including her response to a water load, to intravenous insulin, and to stress). Moreover, though A.C.T.H. 100 mg. daily produced an effect on 17-ketosteroid output and serum-potassium levels of the same order as had appeared intermittently in the preliminary control periods, it produced in addition a profound and sustained eosinopenic response. Clearly 11,17-oxysteroid production was not deficient in this patient either under ordinary conditions or in response to A.C.T.H.

DISTURBANCE OF ELECTROLYTES

It has long been recognised that adrenocortical hyperplasia in infants may be accompanied by excessive loss of sodium and that, though this is corrected as the child grows older, it tends to recur during infections. In Cushing's syndrome a low serum-potassium level is sometimes seen ; and this may be sufficiently severe to produce the hypochloræmic alkalosis which is now recognised to follow a potassium deficit. It is assumed that this hypokalæmia is due to the excessive production of a steroid with a deoxycortone-like action. In this patient the low serum-potassium levels presumably resulted from the same cause.

Occasionally this hypokalæmia was accompanied by a serum-sodium level above normal ; but, although examined on scores of occasions, no reduction of plasma-chloride level and no increase of CO_2-combining power beyond average limits were recorded. The hypokalæmia was not accompanied by fatigue, muscle weakness, or electrocardiographic change. This lack of correlation is now widely recognised. Since this observation of hypokalæmia in the adrenogenital syndrome has apparently not been made before, great care was taken to ensure that these results were accurate. They were checked against estimations made on other patients on the same day, they were frequently estimated by different methods, and they were usually duplicated in two laboratories.

In another patient with adrenocortical hyperplasia now being investigated a similar hypokalæmia has been observed :

A school-mistress, aged 24, complained that a considerable growth of hair had been present on her face since adolescence. She had a male distribution of hair on her abdomen. Her menarche was at the age of 18, and her menses are scanty, short, and irregular. Her breasts are normally developed, and her clitoris is moderately enlarged. Her average daily excretion, determined each day for 23 days, was 21·3 mg., the lowest daily value being 11 mg. and the highest 30 mg. The average daily serum-potassium level in a month was 14·3 mg. per 100 ml. (3·7 m.eq. per litre), and the average of seven daily serum-potassium levels obtained in another laboratory in the same period was 14·4 mg. per 100 ml. (3·7 m.eq. per litre).

POSSIBILITIES OF THERAPY

Though the treatment of adrenocortical hyperplasia in childhood, whether in female pseudohermaphroditism or in macrogenitosomia præcox in boys, is undeniably first-class therapy, it is uncertain whether adrenocortical hyperplasia occurring at puberty and after justifies continued treatment with cortisone. The suppression of the signs of virilism—hirsuties, menstrual disturbance, acne, and so on—may seem to be an inadequate reward for the frequent injections of a potentially hazardous substance. On the other hand, few conditions cause more distress to girls in adolescence and in young womanhood than does virilism, and, when cortisone is more freely available, such therapy, carefully controlled, may justifiably be practised. This condition is by no means rare and, since its effective treatment will require about 20 *g.* of cortisone a year, such therapy is not immediately practicable.

SUMMARY

The treatment of a patient with the adrenogenital syndrome (virilism) with cortisone for five months is described.

The amount of cortisone required for the suppression of excessive androgenic activity was about 50 mg. daily. This dosage slowed the rate of facial hair-growth by about half.

The finding of intermittent hypokalæmia in this patient and in another with the adrenogenital syndrome is reported. This parallels the potassium deficit which sometimes occurs in the adrenocortical (Cushing's) syndrome.

This paper is the report of a great deal of investigation, much of it here unrecorded, conducted by several technicians. The chemical investigations were made in the laboratory of the Derbyshire Royal Infirmary (Dr. G. R. Osborn) by Mr. J. A. Allen, Miss A. Matthews, B.SC., and Miss J. Pegg, B.SC. The duplication of the potassium estimations was done in the laboratory at the Sheffield Royal Infirmary (Dr. A. Jordan) by Mr. D. A. Podmore, A.R.I.C., Miss K. P. M. Groocock, B.SC., and Miss M. C. O'Connell, B.SC. The estimation of 17-ketosteroids was done by Mr. F. Mitchell, B.SC., in the laboratory of the Jessop Hospital for Women, Sheffield (Dr. G. C. Paine). To all these chemists my thanks are due. Dr. Harold Tulloh and Dr. Barbara Green, my house-physicians, and Miss L. M. Edwards, my ward-sister, gave me much help. I am indebted to the Medical Research Council for the A.C.T.H. and the cortisone.

REFERENCES

Bartter, F. C., Albright, F., Forbes, A. P., Leaf, A., Dempsey, E., Carroll, E. (1951) *J. clin. Invest.* **30**, 237.
Bishop, P. M. F., Bray, B. M., de Mowbray, R. R., Merivale, W. H. H., Vaughan-Morgan, J. (1952) *Lancet*, i, 1287.
Koets, P. (1949) *J. clin. Endocrinol.* **9**, 795.
Merivale, W. H. H. (1951) *J. clin. Path.* **4**, 78.
Simpson, S. L. (1952) *Lancet*, ii, 91.
Wilkins, L., Gardner, L. I., Crigler, J. F. jun., Silverman, S. H., Migeon, C. J. (1952) *J. clin. Endocrinol.* **12**, 257.
— Lewis, R. A., Klein, R., Gardner, L. I., Crigler, J. F. jun., Rosemberg, E., Migeon, C. J. (1951) *Ibid*, **11**, 1.

THIOPENTONE FOLLOWED BY NITROUS OXIDE AND OXYGEN FOR ANÆSTHETISING OUTPATIENTS

E. HARVEY FRANKS
M.B. Lond., D.A.
LATE RESIDENT ANÆSTHETIC REGISTRAR, BEDFORD GROUP OF HOSPITALS

UNTIL recently a blind eye was turned on the unsatisfactory conditions associated with general anæsthesia for ambulant patients. In no other type of anæsthesia were anoxia and poor operative conditions permitted, but in the casualty department these were looked on as inevitable. Bourne (1951) tried to prevent anoxia and struggling by using cyclopropane instead of nitrous oxide, and was impressed by the results. Rook (1952) emphasises the advantages of a short-stay ward attached to the casualty department; outpatients can then be given full premedication followed by adequate general anæsthesia. Franks (1952), however, points out that very few hospitals possess a short-stay ward, and that the length of stay in hospital required by this technique is a disadvantage.

In busy outpatient departments rapid recovery and early return home are outstanding considerations, and this is why nitrous oxide still remains the most commonly used anæsthetic agent for outpatients in this country. Though in many cases patients can be anæsthetised satisfactorily with nitrous oxide, in others it fails badly. In anæsthetic-resistant patients a smooth anæsthesia with good operative conditions cannot be obtained unless the gas-and-oxygen is reinforced or superseded by a more potent agent. It is over the choice of the potent agent that disagreement arises.

DISADVANTAGES

The disadvantages of various techniques of general anæsthesia for outpatients are as follows:

Nitrous Oxide—Air.—Adequate oxygenation cannot be maintained, and length of administration is limited.

Nitrous Oxide—Oxygen.—It may be impossible satisfactorily to anæsthetise resistant patients. Anoxia may be unavoidable.

Nitrous Oxide—Oxygen—Trichlorethylene.—This is a very useful technique but may produce breath-holding or a bout of coughing in heavy smokers.

Cyclopropane—Oxygen.—The main disadvantages of this method are that it is inflammable and cannot be trusted to the novice. Postoperative nausea and vomiting may be troublesome.

Intermittent Thiopentone.—Recovery may be slow and be associated with disorientation. The practice of shortening the recovery period by *routine* injection of an analeptic does not appear rational.

Full Premedication and General Anæsthesia.—A short-stay ward is essential, and the patient's stay in hospital is very long after even minor surgical procedures.

THIOPENTONE—NITROUS OXIDE—OXYGEN

Various methods of general anæsthesia have been tried in the casualty department of the County Hospital, Bedford, and that described below has been found the most successful. It is not a new technique; its use in resistant dental cases has been described by Macintosh and Pratt (1940). It has been used here in more than two hundred consecutive and unselected adult outpatients, and has shown its best results in the anæsthetic-resistant and in the poor-risk patients in whom anoxia is particularly undesirable. This method allows optimal oxygenation of the tissues and thus enables nitrous oxide to produce its best degree of muscle relaxation (Guedel 1951). It is assumed that, if 17–20% oxygen is administered throughout the major part of the anæsthesia, anoxia is either minimal or absent.

The method consists of a sleep-dose of thiopentone followed by nitrous oxide/oxygen anæsthesia. It is based on the synergistic action between these agents shown by Organe and Broad (1938), who observed that administration of about 85% nitrous oxide and 15% oxygen halved the amount of barbiturate required to produce anæsthesia.

Premedication.—Atropine gr. $^1/_{100}$ is used in all the cases to prevent excessive salivation and to reduce thiopentone-irritability of the larynx.

Assessment of Patient.—Each patient is classified according to age, physique, occupation, habits, &c., as "frail," "average," or "resistant," and the dose of thiopentone varied accordingly.

Sleep-dose of Thiopentone.—The amount needed by most patients is 2–5 ml. of the 5% solution (0·10–0·25 g). This amount is, of course, inadequate to produce anæsthesia. In making the injection 0·5 ml. is given and, after a slight pause during which the patient is asked if he feels any discomfort, the remainder of the selected dose is injected *rapidly*.

Inhalational Supplement.—As soon as the patient has become unconscious, several breaths of pure nitrous oxide are given, after which oxygen is introduced in increasing concentration. Gas-and-oxygen is administered for about two minutes before the operation begins, so as to produce some degree of nitrous oxide saturation in the tissues. After the skin incision, &c., the oxygen can usually be increased to, and maintained at, 17–20% without reflex movements or other signs of lightening anæsthesia. The Walton III machine has been used without rebreathing, the percentage of the inspired gases being read off from the dial directly.

Recovery.—Consciousness is regained well within a minute, but sometimes a patient appears to remain asleep at the end of this time; he will, however, open his eyes if addressed loudly and soon begins to talk rationally. There seems to be little tendency to fall asleep again unless the dose of thiopentone has been excessive. There is a striking absence of excitement on coming round. Nausea and vomiting are uncommon, as indeed are other ill effects. A few patients complained afterwards of headache, but in these the dose of thiopentone was probably excessive. Many patients remarked on the pleasantness of the anæsthetic. Most patients were able to leave hospital in about half an hour by public transport, often unaccompanied.

Range of Use.—The technique has been used for all the common outpatient operations, except those on the face. The length of the operations varied from $1^1/_2$ to 28 minutes. The technique is indicated especially in anæsthetic-resistant and poor-risk cases.

RESULTS

This method has been used in more than two hundred consecutive adult patients, and data have been collected in the last hundred of these. Of these hundred patients 14 were classified as frail, 71 as average, and 15 as resistant. Their ages varied from 18 to 89, and twelve patients were over 70. The average dose of thiopentone was 3·75 ml. of the 5% solution, with a range of 1·5–7·0 ml. Only 2 patients required more than 5 ml. The average oxygen proportion for the major part of the anæsthesia was 19%, and the average time to leave hospital was $28^1/_2$ minutes, with a range of 15–50 minutes. 55% went home unaccompanied and without incident. The post-anæsthesia vomit-rate was 6%. In no case was there regurgitation after the thiopentone. This was prevented by giving the patient's stomach plenty of time to empty before induction, by keeping his head slightly elevated on a pillow, and by using only very small doses of thiopentone. Operative conditions were excellent in most cases, and satisfactory even in resistant patients. Anoxia seemed to be either absent or only slight.

I wish to thank Dr. M. D. C. Hosford, consultant anæsthetist to the Bedford group of hospitals, for his very helpful

criticism and advice in the preparation of this paper; and the casualty staffs for their coöperation.

REFERENCES

Bourne, J. G. (1951) *Brit. med. J.* i, 1330.
Franks, E. H. (1952) *Lancet*, i, 1259.
Guedel, A. E. (1951) Inhalation Anesthesia. New York; p. 51.
Macintosh, R. R., Pratt, F. B. (1940) Essentials of General Anæsthesia. Oxford; p. 86.
Organe, G., Broad, R. J. B. (1938) *Lancet*, ii, 1170.
Rook, J. R. (1952) *Ibid*, i, 1202.

TETRAETHYL LEAD POISONING

REPORT OF A NON-FATAL CASE

GEOFFREY WALKER
M.B. Lond.
FORMERLY HOUSE-PHYSICIAN, PROFESSORIAL MEDICAL UNIT, MIDDLESEX HOSPITAL, LONDON

PHILIP R. BOYD
M.B. Lond.
SENIOR MEDICAL OFFICER, ASSOCIATED ETHYL COMPANY LTD.

THE following history is typical of tetraethyl lead (T.E.L.) poisoning.

The patient was foreman of a gang of men employed to remove the T.E.L.-containing sludge from large storage tanks which had contained leaded petrol, and although he seems to have been familiar with the stringent safety precautions required in such work he apparently omitted to observe some of them.

A brief account is also given of another five men similarly exposed to the same hazard.

CASE-RECORD

Case 1.—A man, aged 26, had cleaned petrol tanks since December, 1949. He worked about thirty-five hours each week with frequent short daily rest periods in the open air. Inside the tank he wore protective boots and gloves and an oilskin suit, but admitted that sometimes he had not worn the positive-pressure air-line respirator provided as an essential part of his equipment. He explained that it made manual work uncomfortably hot, and slower for his gang than his ambition to prove himself an efficient foreman would permit. He claimed to have observed all the other precautions required in his occupation, such as washing before meals and after work each day, bathing and changing his clothes regularly, and drinking a pint of milk each day; but he admitted that his unprotected face was sometimes splashed by the sludge. He was twice clinically examined by local doctors, on Aug. 24, 1950, and Feb. 12, 1951. On both occasions he was found healthy, and on the latter occasion was told that no signs of lead absorption were detected.

The following history was compiled with the help of the patient's diary. In early February, 1951, he first experienced difficulty in falling asleep and in concentrating on the administrative side of his work. He was worried about his wife's health and about debts resulting from excessive beer-drinking. Later the same month he abruptly stopped drinking. By March 9 he was so despondent that he decided to absent himself from work for a few days, but he was recalled the same evening. The next day he heard that one of his men had become insane; and on his own initiative he stopped work and took his men to London, where he reported to his employers. On March 11 the gang left for another site, and that evening he overheard the men debating whether or not to tell him of the sudden death of one of their workmates, allegedly from a brain tumour. They had apparently noticed that he was depressed and listless and did not wish to upset him further. He immediately became very anxious and wished to visit a church. Instead he went to see a doctor, who reassured him and sent him back to his lodgings. Anxious to be with his wife, who was then on holiday 100 miles away, he set out to walk to her, without any idea of the appropriate route. A lorry driver picked him up, soaked to the skin, and drove him to London, where he found his way to his own home. Subsequently he was taken by his wife to a hospital where, after an examination, he was reassured and sent home. On March 15 his employers, who suspected T.E.L. poisoning, arranged for him to be admitted to the Middlesex Hospital.

On admission he was obviously worried and talked about himself for two hours, quoting extensively and haphazardly from his diary. He was anxious about his wife's health, and explained that he felt that he was responsible for the death of one, and the illness of another, of his men by failing to insist on precautions which he had known were necessary in their work. He said that for 2 weeks he had experienced twitching of the nose, a feeling of something stuck in the throat, a creeping sensation in the region of the right ear and shoulder, transient blurring of vision, and episodes of what appeared to have been experiences of *déja vu*. He had also had insomnia, relieved by hypnotics, for over 3 weeks, and since admission he had experienced panicky feelings of instability. He complained of halitosis and a metallic taste in his mouth for a few days. His appetite had become voracious, but he claimed to have lost about 14 lb. in weight during the last month. He had recently complained of a mild sore throat and occasional headaches but had had no fits or faints and no disturbance of bowel habit. The family and past medical history revealed nothing which seemed relevant.

On examination he appeared intensely anxious, but the physical signs usually associated with anxiety were strikingly absent. His temperature was 97·4°F; pulse regular, rate 68 per min.; and blood-pressure 105/45 mm. Hg. His palms were warm but dry; there was no tremor of his outstretched hands; and his pupils were not dilated. His tendon-reflexes were symmetrically brisk, and there was no "lead line." There were no other physical signs of disease, except a large blister on the left big toe—evidence of his long walk. He weighed 164 lb.

Examination of the blood showed Hb 13·3 g. per 100 ml., red cells 5,000,000 per c.mm., colour-index 0·95, white cells 7400 per c.mm. (neutrophils 45%, lymphocytes 44%, monocytes 5%, eosinophils 6%). No basophilic stippling of erythrocytes was seen.

Urine.—Tests for reducing substances, coagulable protein, and blood were all negative.

Lumbar puncture produced clear cerebrospinal fluid at a pressure of 105 mm. (rising freely to 185 mm. on jugular venous compression) and containing protein 30 mg. per 100 ml., sugar 61 mg. per 100 ml., chloride 692 mg. per 100 ml., and 1 lymphocyte per c.mm. A Pandy test was negative, and a Lange test gave 0000000000.

Liver-function Tests.—A colloidal gold test was negative. Thymol turbidity was 3 units. The serum-bilirubin level was 0·3 mg. per 100 ml. The alkaline phosphatase level was 2·7 King-Armstrong units, and the cholesterol level 174 mg. per 100 ml.

Urinary Lead *.—The corrected urine-lead levels were 0·36 mg. per litre on March 15; 0·24 mg. per litre on April 10; 0·23 mg. per litre on April 22; and 0·21 mg. per litre on April 23. The normal urinary excretion of lead is 0·06–0·08 mg. per litre (Kehoe et al. 1935).

Chest radiography and electrocardiography showed no abnormality.

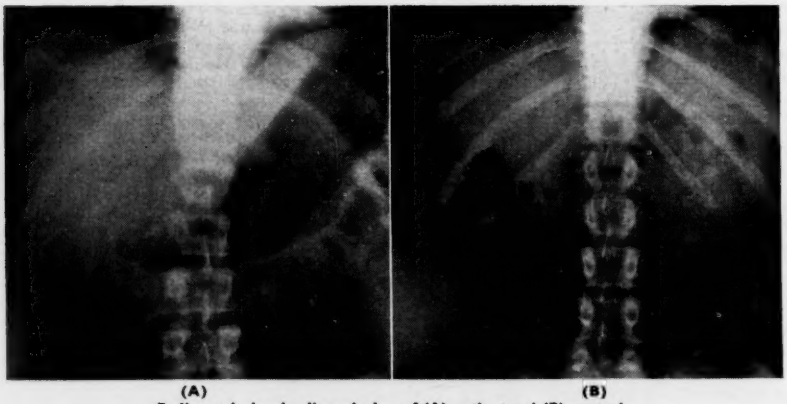
Electro-encephalography and abdominal radiography are discussed below.

Treatment was entirely conservative. For the first week the patient was confined to bed, encouraged to drink five or six pints of fluid daily, and given phenobarbitone gr. 1 four times daily and 'Sodium amytal' gr. 3 at night. Subsequently he was allowed out of bed for progressively increasing periods, and the sedation was reduced. The phenobarbitone was omitted for two days before electro-encephalography.

Progress.—His symptoms gradually disappeared, and when he was discharged on April 14, 1951, he complained only of occasional creeping sensations in the right side of his head and insomnia when the sodium amytal was withheld. During his month in hospital he gained 10 lb. in weight, his pulse-rate was 60–80 per min., and his temperature 97°–98°F. His blood-pressure, known to have been 130/80 mm. Hg in February, 1948, averaged 90/50 mm. Hg during the first week, and increased to 120/60 mm. Hg on discharge.

Follow-up.—He was seen again on April 23 and 24, 1951, when he was admitted overnight for electro-encephalography,

* Lead estimations were done by a short colorimetric method using dithizone on snap samples of urine, and the values obtained were corrected to a standard specific gravity of 1·014 by multiplying by 14/X, where X equals the last two figures of the specific gravity of the urine when the specific gravity of water is expressed as 1·000. This method was adopted to obtain comparable figures over long periods in individual workmen when only snap samples were available. The values it gives are roughly proportional to the rate of excretion of lead.



(A) (B)

Radiograph showing liver shadow of (A) patient and (B) control.

and again about 3 weeks later, after a seaside holiday. At this time he said that he felt very well but still required a hypnotic at night. He proposed to look for alternative employment.

RADIOGRAPHIC DEMONSTRATION OF LEAD IN THE LIVER

T.E.L. is highly lipoid-soluble, and Kehoe and Thamann (1931) showed that in laboratory animals it is concentrated in lipoid-rich organs, particularly the liver. Cassells and Dodds (1946) confirmed this in two fatal human cases, reporting values of 2·35 mg. and 2·5 mg. of lead per 100 g. of wet liver tissue. At the suggestion of Dr. D. Sutton that such lead concentrations in the liver might be demonstrable radiographically, the patient and three healthy medical students of similar girth were radiographed with identical exposures, and the plates were developed under identical conditions. The patient's liver shadow was denser than that of the controls (see figure). That this difference can be due to the presence of lead in the liver was confirmed by taking radiographs, under identical conditions, of a glass tank containing water, and then an aqueous solution of lead acetate containing 2 mg. of lead per 100 ml. The shadow of the lead solution was appreciably denser than that of the water alone. Lack of other patients has so far prevented extension of this work.

ELECTRO-ENCEPHALOGRAPHY

Electro-encephalography on March 27, 1951, showed a slow α rhythm of 8 per sec., which was disturbed in all areas by runs of 5–6 per sec. waves, seen most obviously in the central part of the right temporal lobe. Hyperventilation caused the appearance of paroxysms of 2 per sec. waves in both frontal regions and some 3 per sec. activity over the rest of the cortex.

By April 24, 1951, the record had changed considerably, the dominant frequency varying between 7 and 9 per sec., its voltage having doubled from 16 to 32 μ. In the first record the recordings from the parietal region were relatively flat and featureless, whereas in this record the 7 per sec. frequencies were predominant. In the temporal lobes the previous asymmetry was reproduced and, as elsewhere, had a higher voltage. The response to hyperventilation was also different: within half a minute low-voltage 2 per sec. waves appeared in both occipital regions. High-voltage generalised 3–4 per sec. waves first appeared at $1^1/_2$ min. and appeared paroxysmally for the rest of the exercise of $3^1/_2$ min. and for 20 sec. after it. They had not appeared in the previous record until 2 min. 20 sec., and on that occasion were not nearly so well marked.

We have not been able to find any published work on the electro-encephalogram in T.E.L. poisoning in man; but Hill and Parr (1950) mention the unpublished finding that the changes resemble those seen in the early stages of T.E.L. poisoning in cats, which Steinman and Therman (1939) describe as a decrease in amplitude of cortical rhythm, with a tendency to cortical instability. Our findings, which conform with these, suggest that in man T.E.L. causes generalised suppression of cortical activity, with the appearance of non-specific slow-wave activity.

DISCUSSION

The anti-knock properties of T.E.L. were discovered by Midgley and Boyd (1922), and manufacture and blending with petrol began in America in 1924. The toxicity of the substance was not recognised until many workmen died, when manufacture was suspended for a year, pending the result of a government inquiry. It was resumed only after the enforcement of strict industrial and medical controls which made the industry safe. There have been no deaths since manufacture and blending started in England in 1940. Apart from isolated cases, such as those reported by Cavallazzi (1946), where poisoning followed exposure to an insecticide, and those of Bini and Bollea (1947), where workers cleaning clothes with leaded petrol were involved, the only cases reported recently in America and Western Europe have occurred in tank cleaners. These men work in small parties and, in spite of supervision, have in each incident relaxed the precautions necessary for their safety. Such an outbreak in England was reported by Cassells and Dodds (1946).

T.E.L. is absorbed chiefly through the skin and the respiratory tract, and waterproof clothing and respirators of various types afford complete protection. Hence, when proper equipment is available and is in working order, tank cleaning should be entirely safe, outbreaks of poisoning being due to the negligence of the workmen.

The clinical picture of T.E.L. poisoning was reviewed by Machle (1935). The symptoms are referable chiefly to the nervous and alimentary systems. Insomnia, lassitude, irritability, and unpleasant dreams appear early, and may be followed by weakness, tremor, and headache. Anorexia and loss of weight are common, and nausea, morning sickness, and diarrhœa may occur. In severe cases a toxic psychosis develops, with hallucinations, delusions, and excitement which may terminate fatally in delirium. If recovery takes place it is usually complete, and sequelæ are uncommon. The characteristic physical signs are pallor without anæmia, low temperature, bradycardia, hypotension, and brisk tendon-reflexes. In severe cases collapse and encephalopathy are found. Lead line, neuropathy, and basophilic stippling of the erythrocytes are rare in contradistinction to inorganic lead poisoning.

The diagnosis is established from a history of exposure, the clinical picture, and urinary lead estimations. Mild cases give urinary concentrations of about 0·2 mg. of lead per litre, and severe cases up to 4 mg. per litre. The clinical picture, however, does not always run parallel with the urinary excretion of lead.

The most widely accepted treatment is conservative. Good nursing, sedation, and the maintenance of a high intake of fluid are essential. R. Kehoe (personal communication) states that there is little evidence that the course of the disease has been materially influenced by

the use of dimercaprol. No results have so far been published on the effect of di-sodium phosphate, recommended by Proctor and Kahn (1950) to accelerate the excretion of lead in inorganic lead poisoning.

The development of symptoms within a few days of stopping heavy drinking of beer, noted in case 1, was also noticed by Benassi (1939) in his fatal case. No explanation is offered.

NOTES ON OTHER CASES

Case 2.—A single man, exposed in a similar fashion to case 1, after a few days of insomnia and restlessness, became confused, deluded, and aurally hallucinated, and was certified insane on March 9. On admission to a mental hospital his temperature was 97·6°F and his blood-pressure 105/80 mm. Hg. No physical signs of organic nervous disease were found, but moderate albuminuria and hæmaturia were present. His mental condition gradually improved, and he was fit for discharge after 6 months.

Case 3.—A man, who had twice sought medical advice for insomnia and weakness, collapsed on March 7 and was admitted to hospital. He was very agitated and complained bitterly of a sore throat, although only minor faucial injection could be seen. 2 days later he became hallucinated and increasingly restless and died after a convulsion. At the time of his death his occupation seems to have been unknown, and the diagnosis of T.E.L. intoxication was not considered. The history of exposure and the subsequent clinical picture, however, strongly support the possibility of T.E.L. poisoning, although confirmatory biochemical evidence is not available.

Three other men, who had minor symptoms of sleeplessness and restlessness but no physical signs, were found to have an abnormally large amount of lead in the urine and undoubtedly had mild T.E.L. poisoning.

SUMMARY

A non-fatal case of tetraethyl lead poisoning in a petrol-storage tank cleaner is reported, with notes on other affected men.

Observations are made on the electro-encephalographic changes and on the increased density of the liver shadow demonstrated radiographically.

We wish to thank Prof. A. Kekwick for his encouragement and permission to report the case, which was under his care; Dr. D. Sutton, who suggested and provided the facilities for the liver radiography; Dr. G. Parsons Smith, who interpreted the electro-encephalograms; and Dr. W. T. Earlam, under whose direction the urinary lead was estimated.

REFERENCES

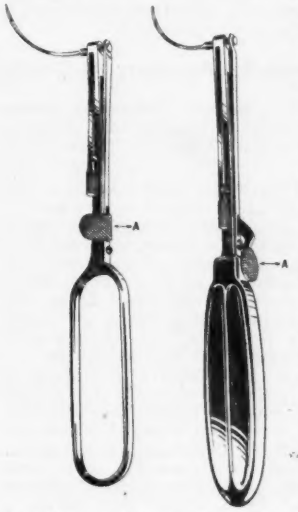
Benassi, G. (1939) *Rass. Med. indust.* **10**, 390.
Bini, L., Bollea, G. (1947) *J. Neuropath.* **6**, 271.
Cassells, D. A. K., Dodds, E. C. (1946) *Brit. med. J.* ii, 681.
Cavallazzi, D. (1946) *Med. Lavoro*, **37**, 367.
Hill, J. D. N., Parr, G. (1950) Electro-Encephalography. London.
Kehoe, R. A., Thamann, F. (1931) *Amer. J. Hyg.* **13**, 478.
— — Cholak, J. (1935) *J. Amer. med. Ass.* **104**, 90.
Machle, W. F. (1935) *Ibid*, **105**, 578.
Midgley, T., Boyd, T. A. (1922) *Industr. Chem. Engng.* **14**, 589, 849, 894.
Proctor, C. D., Kahn, H. S. (1950) *Amer. J. med. Sci.* **219**, 316.
Steinman, S. E., Therman, P. O. (1939) *Amer. J. Physiol.* **126**, 636.

"Some people think that the philosophy a scientist accepts is not of very much importance; his job is to observe the phenomena. This is a gross oversimplification, and it involves the subsidiary hypothesis that all scientists are fully equipped with serendipity. A sensible philosophy controlled by a relevant set of concepts saves so much research time that it can nearly act as a substitute for genius; it may be that this is what we mean by genius. Thus equipped we avoid the pseudo-problems or, more correctly, the problems that are real in adjacent fields but pseudo in our own. A scientist can have no more valuable skill than the ability to see whether the problem he is investigating exists and whether the concepts he is using are applicable. But the lure of a concept that clarifies another field is strong and many of us follow it, like the music of the Pied Piper, to our scientific detriment."—N. W. PIRIE, F.R.S., *Science News*, 25, 1952, p. 20.

New Inventions

MODIFICATION OF BONNEY-REVERDIN NEEDLE-HOLDER

FOR the surgeon who uses the Bonney-Reverdin needle-holder, here is a modification which should be found useful. The essential difference is that the needle eye is opened by means of a separate press-button (shown at point A) instead of by compressing the handle.



The chief reason for altering this well-tried instrument is the tendency of the needle eye to be opened by accidental compression of the handle when the needle is being inserted in or withdrawn from tough tissues such as the rectus sheath. The needle either breaks or becomes fouled in the tissue and soon needs repair.

The two needle-holders shown are exactly the same except that one has a solid handle and the other a loop. They are made by Heaton Grogan Co. Ltd., of Clerkenwell.

Assistant Surgeon,
Department of Obstetrics and Gynæcology,
The London Hospital

ROBERT PERCIVAL
F.R.C.S., M.R.C.O.G.

Reviews of Books

William Smellie

The Master of British Midwifery. R. W. JOHNSTONE, C.B.E., M.D., HON. LL.D., professor-emeritus of midwifery, University of Edinburgh. Edinburgh: E. & S. Livingstone. 1952. Pp. 139. 20*s*.

FOUR boys destined to inscribe their names indelibly on the scroll of medical history were born within a period of thirty years and a distance of thirty miles of one another in the county of Lanark—William Smellie (1697), William Cullen (1710), William Hunter (1718), and his brother John (1728). Smellie is almost best known by the pithy and eminently quotable lampoons written by jealous colleagues. How many medical readers remember that he was said to have "monstrous hands fit only to hold horses," but can recall little about his great place in the history of obstetrics? He used his big hands most dexterously, and by his teaching and practice greatly helped to improve the conditions of poor lying-in women, and the clinical teaching of midwifery to midwives and medical students. This short biography is a modern assessment of his work. The author claims that no other man advanced in his lifetime the knowledge and practice of midwifery to an extent in any way comparable with that achieved by Smellie, and in circumstances which would have discouraged someone less heroic. Without powerful friends to help him, without the advantages of a hospital clinic, he attended and taught in the homes of the poor; and by so doing, and by his writings, raised himself to the foremost position in his profession. His case-notes are freely quoted. As the narrative proceeds, describing one difficulty after another, Smellie's personal character emerges. A man of good will, he was kindly and tolerant towards all except those who were pretentious, insincere, or false; and his unselfish devotion to his patients' interests and his great skill and thoughtfulness are

recalled. The remarkable fortitude of his patients is astonishing. Indeed, to us, with our analgesics and our wide choice of anæsthetics, the sufferings which child-bearing women underwent in the 18th century whenever there was any obstetrical complication are almost unimaginable, and show the reasons that inspired James Young Simpson's unwearied search for a safe anæsthetic for childbirth.

The technical details in this important book will fascinate modern obstetricians and midwives, and there is much that will delight the ordinary reader.

An Explaining and Pronouncing Dictionary of Scientific and Technical Words

W. E. FLOOD, M.A., PH.D., lecturer in education (science method) in the University of Birmingham ; MICHAEL WEST, M.A., D.PHIL. London : Longmans, Green. 1952. Pp. 397. 12*s*. 6*d*.

ILLUSTRATED with 1300 thumb-nail sketches and diagrams, 10,000 scientific and technical words in fifty subjects (including such things as building and architecture) are here explained as to a person knowing little or nothing about them. The idea is good but the execution poor. The selection of terms for explanation is uneven, with many omissions and some naïve and even unacceptable definitions (" dog watch . . . 4–6 evening, 6–8 morning " ; " diptera . . . insects with two pairs of transparent wings " ; " Chagas disease . . . carried by bed-bugs " ; &c.). Moreover, the phonetic representation is irritating for two reasons : the accent does not mean that the syllable before it is accented but the syllable after it ; and the letter R is entirely disregarded except when it comes before a vowel or H. On the other hand, this dictionary is a useful one to have on the shelf because it is likely to list words not contained in some other dictionaries.

The Art of Marriage

MARY MACAULAY, M.B., J.P. London : Delisle. 1952. Pp. 97. 7*s*. 6*d*.

THIS is yet another book in a field where supply must surely soon outpace demand. It is sensible and accurate, but adds to the long list of similar works which are neither exceptional nor exceptionable. The half-quotations from older books (extending as far as Ovid's *Art of Love*) which somehow stick in the mind of sex educationists are all here ; so is a good deal of sound advice based on experience. The book has in it most of the factual matter which patients need, and it is at least fully convinced that sexual relationships can and should be pleasurable. For general counselling use it is probably fully adequate.

Medicinal Chemistry

(In 2 volumes.) ALFRED BURGER, associate professor of chemistry, University of Virginia. New York and London : Interscience Publishers. 1951. Pp. 1084. 80*s*. each vol.

THIS work surveys in detail the whole field of the chemistry of medicinal agents for the advanced student of this branch of chemistry or of pharmacology. Interested medical readers will find it full of information on the effect of chemical structure on pharmacological action.

After some general chapters Professor Burger deals with drugs grouped according to their therapeutic uses. Structural chemistry is presented in detail ; syntheses and derivatives are given great prominence, derivatives especially being used to display the relationship between graded changes of molecular structure and alterations in therapeutic or other biological effects. Modes of action and metabolic fate are discussed and methods of testing outlined ; but comments on therapeutic use are brief, and, on occasion, somewhat ill expressed. The major chapters—on such things as analgesics, drugs acting on the cardiovascular system, and antihistamines—are replete with formulæ of active substances, including all the newer derivatives. References, in footnotes, are ample (up to 1951). Some shorter chapters (those on parenteral fluids, expectorants, and antacids, for instance) are rather sketchy, being insufficiently backed with data from modern organic synthetic chemistry.

In the second volume, which deals with hormones and chemotherapy, the steroid hormones are described chemically in great detail, while sex-hormone therapy occupies less than a page. The sections on sulphonamides, antimalarials, organic arsenicals, antibiotics, and antiseptics are full of facts, and theories of their action are well discussed. Drugs used in the chemotherapy of tuberculosis occupy a 20-page section, and the chapter on antiseptics offers a complete survey and ends with a particularly full account of the quaternary ammonium compounds.

It is a notable achievement for a single author to assemble, in two compact volumes, such an enormous amount of relevant chemical information, and to present it in such a pleasing lucid style.

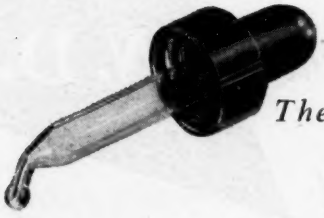
Surgical Gynecology

J. P. GREENHILL, M.D., professor of gynæcology, Cook County Graduate School of Medicine, Chicago. Chicago : Year Book Publishers. 1952. Pp. 350. $8.50.

IN his preface the author states that he has tried to show in as simple a way as possible how to carry out nearly all the gynæcological operations that are being done today. In this he has succeeded most admirably. His text is clear and his exposition definite. Over 100 beautiful pen-and-ink illustrations define each step in the various operative procedures. In addition to the usual operations associated with gynæcology, he describes how to repair injuries to the bladder, ureter, and bowel, and gives an account of the surgical treatment of hæmorrhoids and the repair of inguinal and femoral herniæ. Pitfalls and dangers are mentioned just where they may occur. The book has been carefully prepared and is suitably indexed. It is limited to its title and is not too lengthy. In a future edition the author might consider inserting on each plate of illustrations the name of the operation being described.

Diseases of the Heart and Circulation (2nd ed. London : Oxford University Press. 1952. Pp. 472. 35*s*.). —In its second edition, Dr. A. A. Fitzgerald Peel's useful students' textbook has undergone considerable revision, and —as too often happens with new editions—enlargement. It retains its original merit of correlating clinical cardiology with anatomy and physiology. Unfortunately, its approach to therapeutics is not so commendable. No attempt has been made to differentiate between the treatment of supraventricular and ventricular paroxysmal tachycardia ; and to suggest that amyl nitrite may be of value as a hypotensive agent in hypertension is, to put it mildly, asking for trouble. It is unfortunate, too, that trade names for drugs should be used so profusely, when other teachers are striving to induce their students to restrict themselves to official or approved names. These are minor blemishes in an otherwise commendable book.

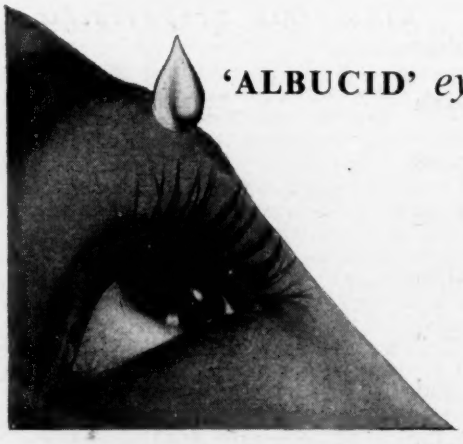
Autopsy Diagnosis and Technic (3rd ed. New York : Hoeber. London : Cassell. 1951. Pp. 471. 45*s*.).—The first edition of this book by Dr. Otto Saphir appeared in 1937, the second in 1946. It was written, in the form of a working manual, to provide a diagnostic outline of the gross lesions most commonly encountered at necropsy. Modifications of the techniques of Rokitansky and Virchow are well described and illustrated, while there is a special section devoted to the examination of stillborns and infants. The chapter on the necropsy permit shows the differences in law and custom between the U.S.A. and the United Kingdom, both in the ordinary and the coroner's examination. These differences—together with the American vogue for embalming the dead—account for the concern of the American pathologist to make use of limited and inconspicuous skin incisions. Dr. Saphir rightly charges the prosector, when he has completed his examination, with the task of explaining the clinical picture in the light of his findings, and of explaining in terms of morphology the various laboratory data collected during the patient's lifetime. The technical parts of the book are very good, but the accounts of the abnormalities found at post-mortem examinations are of questionable value for students, being given more fully in textbooks of systematic pathology. Those with some practical experience of necropsies who are revising pathology, however, may benefit from this form of presentation.



'ALBUCID'

The First name in Ocular Therapeutics

Active against a very wide range of organisms causing ocular infections, 'Albucid' Eye Preparations are known and trusted wherever eye injuries and infections are treated.



'ALBUCID' *eye preparations are available as follows:*

EYE DROPS

Sulphacetamide Sodium B.P. 10%, 20% or 30% in sterile solution, packed with pipette in sealed bottles.
Bottles of 14 c.c. (½ fl. oz.)

EYE OINTMENT

Sulphacetamide Sodium B.P. 2½%, 6% or 10%.
Tubes of 4 Gm. (60 grain) and 25 Gm.

Descriptive literature and samples available on request.

British Schering Limited

229-231, *Kensington High Street, London, W.8.*
telephone: WEStern 8111

SB.1/52

When the worst is over

Skill and care have won the battle, and the exhausted body is recuperating. It is *then* that Burgoyne's Tintara may mean the difference between long, dragging convalescence and a rapid recovery. For Tintara is not only beneficial but a really palatable burgundy. It contains no added alcohol or sugar and is a natural product of sun and ironstone soil.

Burgoyne's

TINTARA

(FERRUGINOUS) PRODUCE OF AUSTRALIA

P. B. BURGOYNE & CO. LTD., DOWGATE HILL, LONDON, E.C.4. TEL: CITY 1616

a mineral-free combined **W.D.P.**

whooping-cough and diphtheria prophylactic

Simultaneous immunization of children against whooping-cough and diphtheria is now widely practised, and reports from various parts of the world have suggested that during the poliomyelitis season it is advisable to avoid a mineral carrier. Pertussis Vaccine and Purified Diphtheria Toxoid are now supplied in combination, in buffered saline, without a mineral carrier.

In sets of 3 × 1 *c.c. doses and in* 10 *c.c. vials.*

(Each 1 c.c. contains 30 L.f. units purified Diphtheria Toxoid (F.T.) with 10,000 millions *H. pertussis*.)

Diphtheria-Pertussis Prophylactic* *is prepared in the Wright-Fleming Institute of Microbiology, St. Mary's Hospital, London, W.2.*

* *Distinguishing mark 'W.D.P.' (in red letters).*

Sole Agents:

PARKE, DAVIS & COMPANY, LIMITED. *Inc. U.S.A.*

HOUNSLOW, MIDDLESEX Telephone: Hounslow 2361

MEDICAMENTA VERA

290

THE LANCET

LONDON: SATURDAY, SEPT. 6, 1952

What of General Practice?

To many students and young doctors the idea of going into general practice makes no notable appeal. For this there are many reasons; but commonly these include ignorance and prejudice. The medical student, trained in scientific method, naturally measures the general practitioner's opportunities by the precise yardstick of science—and shakes his head. What may escape him is that the good family doctor laces science's cold portion with the warmer stuff of humanism. Some of this humanism is being formalised in the doctrine of social medicine, which is finding its way into curricula; but, even so, the general practitioner's twofold technique remains essentially empirical, and only those who have tried know the difficulties and satisfaction of applying it. The ivory hospital of the medical school gives little clue to the medical life beyond its walls. As one practitioner puts it in a letter that we print this week:

> "There are many who can think only of the team around the bed in the great teaching hospital, where the personal onus of care is not so heavily on one man, where the relatives are not watching each move and action, and where the patient's friends do not have to be met and spoken to each day."

The student's prejudice against general practice derives partly from the influence of his teachers. Last week, in his good-natured tilt at academic training, Dr. BROMLEY [1] observed that this is the age of the medical don. Dons, especially those who pursue scientific disciplines, are not remarkable for their tolerance of the empirical; and thus, unknowingly, academic teachers may turn their students against a career beyond the university or large hospital.

The upshot is evident from an article that appeared a week or two ago in our unconstrained Points of View series. Here an anonymous correspondent [2] outlined in darkest colours his conception of general practice. Now others of his generation may not see the picture so black; but we believe that many see it in varying tints of grey. Our correspondent hinted at this. "So it is," he concluded, "that the queue for specialisation grows and grows, and those that at last sink into general practice are bitter and frustrated near-specialists, hating themselves and their job."

Such hostility is best eradicated by giving the facts; and an increasing number of medical schools are shrewdly enabling students to meet practitioners and to see practices.[3] The sort of information that such contacts may yield is indicated in the letters that we publish this week in reply to our correspondent's, perhaps deliberately, provocative arguments. Conditions for the practitioner are far from perfect; but they are not nearly so inimical as some have supposed. Together, these letters show that general practice is emphatically a live concern; and Dr. BALL suggests that the National Health Service Act, far from hastening its end (as many with keen *Schadenfreude* have proclaimed), has in some ways given it new strength. For example, the shadow of fees no longer inhibits doctor or patient; the heavy task of buying a principal's place no longer weighs on the young doctor; and clerical work is, if anything, lighter than before. Furthermore it seems that the rift between hospital and practitioner is being partly bridged by an increasing number of hospitals that are wisely opening their investigation departments to the family doctor, who thus retains more patients continuously in his charge. Then again, the Danckwerts award at last promises adequate pay. Though this alone will not bring suitable candidates, it is one important factor.

We believe that more good candidates will come forward—and come forward eagerly—if students are convinced of the importance of general practice to our society. Unfortunately, general practitioners, who already appreciate this, seldom say so—our correspondence columns this week provide a welcome exception. A college or faculty of general practice [4] could do much to attract to this indispensable and rewarding work a fair share of the profession's best skill.

1. Bromley, J. F. *Lancet*, Aug. 30, 1952, p. 393.
2. *Ibid*, Aug. 16, 1952, p. 332.
3. See leading article, *Ibid*, 1952, i, 495.

Isoniazid Trials

A FEW weeks ago, discussing bacterial resistance to isoniazid, we suggested that there seemed no justification for using this substance alone in preference to streptomycin and *p*-aminosalicylic acid (P.A.S.), except in planned clinical trials.[5] GRACE and his colleagues [6] now suggest that it should not be used alone even for large-scale clinical tests. As such tests are at present being carried out by the Medical Research Council in this country, by the Veterans Administration and the Public Health Service in the U.S.A., and by the National Association against Tuberculosis in Sweden, this view needs to be carefully considered.

The evidence on which it is based is derived almost entirely from laboratory experiments. GRACE et al. point out that isoniazid is the only commercially available antibacterial agent, apart from streptomycin, against which bacteria can become almost completely resistant in a single step. Furthermore, in vitro, resistance to isoniazid originates about 1000 times as rapidly as resistance to streptomycin. The advantages of administering more than one antibacterial substance are evident in many diseases; and mutation to resistance against two drugs given together is theoretically the product of the individual mutation-rates. In the case of isoniazid and streptomycin it has been calculated that a volume of bacteria almost as great as that of the human body would be necessary for the finding of a cell simultaneously resistant to both agents. GRACE and his colleagues predict the early and widespread appearance of resistant strains if isoniazid continues to be used alone, and this will

4. See leading article, *Ibid*. p. 139; Hunt, J. H. *Ibid*, p. 1303.
5. Leading article, *Ibid*, p. 1293.
6. Grace, E. J., Bryson, V., Szybalski, W., Demerec, M. *J. Amer. med. Ass.* 1952, **149**, 1241.

largely neutralise "one of the most hopeful developments in the recent history of tuberculosis therapy"; trials of isoniazid alone are "nothing short of catastrophic."

This argument seems to be based on several assumptions: that isoniazid is a very effective agent against tuberculosis in man, that resistance to it is clinically significant and permanent, and that combination with other drugs will prevent resistance. None of these assumptions has so far been proved. The original reports on isoniazid suggested that it is remarkably effective against tuberculosis in man; but this has not been conclusively demonstrated. Furthermore, the clinical significance of resistant strains emerging during treatment is difficult to determine. The emergence of variants highly resistant to streptomycin tends to worsen the prognosis; but strains of relatively low resistance may have little or no clinical significance.[7] Although highly isoniazid resistant strains can be produced in the laboratory, the resistance of strains so far reported in the sputum during treatment has been relatively low.[8] Highly resistant variants will probably be found as investigation continues, but it cannot be assumed that they will necessarily have the same significance as with streptomycin. Certainly there is already a hint that isoniazid resistance may be of some importance, since the number of bacilli in the sputum begins to increase after its appearance[8]; but this feature has been observed during streptomycin treatment, even when the variants which have emerged show such low resistance that this in itself may be clinically insignificant.[9] Furthermore, in vitro, resistance to isoniazid is certainly not permanent. Strains which appear resistant can become sensitive when grown in isoniazid-free media[10]—a reversion which does not take place with streptomycin-resistant variants. As GRACE and his colleagues point out, there is still no indication that this reversion occurs in the body when isoniazid is stopped; but there is also no evidence that it does not occur. Very little is known about combinations of isoniazid with other drugs. Exposure of tubercle bacilli in vitro to isoniazid with streptomycin apparently delays or averts bacterial resistance to both[11–13]; but we do not know whether other combinations behave similarly.

In the absence of so many essential facts we cannot accept the conclusions of GRACE and his colleagues. But, supposing that the dangers they foresee are real, can continuation of the trials still be justified? An effective, relatively cheap drug that can be administered for long periods by mouth would be of immense value. Treatment with streptomycin and P.A.S. is still expensive, and, except under close supervision, difficult to carry out in the patient's home. In large areas of the world the only chance of helping the great majority of patients is by developing a form of antibacterial therapy readily obtainable by all. It seems right, therefore, to explore fully the potentialities of isoniazid even in the face of early reports of bacterial resistance and knowledge of what this might signify. Without controlled trials of isoniazid alone the efficacy of this drug cannot be proved, nor can its effect be measured against the known action of others. The action of streptomycin and P.A.S. alone and combined has been fully investigated, particularly by the Veterans Administration in the U.S.A. and by the Medical Research Council in this country. Because of the planned continuity of the M.R.C. investigations it may perhaps be possible to compare the effects of isoniazid with those of streptomycin and P.A.S. alone and combined. Such basic knowledge would have much value. GRACE and his colleagues suggest that administration of isoniazid should be combined with, for example, streptomycin and P.A.S.; but the immediate clinical effect of the three drugs together is unlikely to be much greater than that of streptomycin and P.A.S. only. Thus to show the differences convincingly would require very large numbers of patients with long delay in completing the trials. Moreover, the important question whether isoniazid can be used effectively by itself would remain unanswered. Only properly conducted clinical trials can quickly and convincingly prove that isoniazid should not be used alone. Warnings based on *a priori* reasoning are unlikely to prevent the widespread use of such a simply administered, cheap, and plentiful drug in a disease such as tuberculosis. Facts are required; and these can come only from efficiently conducted clinical trials.

At the same time, on the evidence so far brought to light, the potential dangers of bacterial resistance are real enough to justify a very strong warning against its indiscriminate use in ordinary practice, either alone or with other antibacterial drugs. Streptomycin and isoniazid together are already being investigated under controlled conditions, and we hope that isoniazid and P.A.S., which form an attractive combination because of its easy administration, will also be tested in this way. Until the results of these trials are known it seems reasonable to give it together with, rather than instead of, streptomycin and P.A.S. Voluntary restraint in the exploitation of this new and probably valuable drug can prevent any serious dangers from bacterial resistance.

7. Daniels, M., Hill, A. B. *Brit. med. J.* 1952, i, 1162.
8. Steenken, W. jun., Meade, G. M., Wolinsky, E., Coates, E. D. *Amer. Rev. Tuberc.* 1952, **65**, 754.
9. Bignall, J. R., Clegg, J. W., Crofton, J. W., Smith, B. J. D., Holt, H. D., Mitchison, D. A., Armitage, P. *Brit. med. J.* 1950, i, 1224.
10. Pansy, F., Stander, H., Donovick, R. *Amer. Rev. Tuberc.* 1952, **65**, 761.
11. Middlebrook, G. *Ibid.* p. 765.
12. Szybalski, W., Bryson, V. *Ibid.* p. 768.
13. Knox, R., MacLean, K. S., Robson, J. M. *Brit. med. J.* 1952, i, 1081.

Atropine Alkaloids

PHYSICIANS, no less than metaphysicians, must often wonder why the vegetable kingdom contains well-defined chemical substances with specific actions on man and animals—actions which can often be turned to good therapeutic account. Many vegetable drugs still hold their own. We are hard put to it to improve on morphine, ergometrine, digoxin, and emetine, to mention only a few. Pharmacists spend a good deal of time and energy (to say nothing of money) in trying to improve on Nature. Their purpose is to enhance the therapeutic usefulness of a drug and at the same time to diminish its side-effects. Whether they succeed or fail they usually throw new light on the action of the drugs they investigate.

The deadly nightshade, *Atropa belladonna*, is a good example. Some of its actions have been known for centuries, but modern developments in the chemistry and pharmacology of its alkaloids date from the isolation of atropine by MEIN in 1831. The structure

of the atropine group of alkaloids offers almost unlimited scope to the chemist. They are esters formed by the union of an aromatic acid (tropic acid) with organic bases (tropine or scopine). The substitution of other acids and bases has yielded a crop of synthetic compounds, many of which have come to the notice of doctors in recent years. Yet, although many of these new drugs have established their claim to official recognition, the indications for their administration in preference to atropine or hyoscine are rather limited. Moreover, existing atropine substitutes are likely to be constantly challenged by new arrivals. Homatropine (tropic acid plus mandelic acid) has, however, almost certainly come to stay—at any rate among ophthalmologists—and in the United States eucatropine, the mandelic acid ester of a polymethyl piperidine derivative, is put to similar uses. Other synthetic compounds have been designed to give maximum relaxation of smooth muscle with minimum effects on the eye, the salivary glands, and cerebral function. One of this group is amprotropine phosphate ('Syntropan') (the tropic acid ester of 3-diethylamino-2, 2-dimethyl-1-propanol), which is intended to relieve painful spasm in the hollow viscera—the intestine, bile-duct, bladder, and ureters. The structure of 'Trasentin' is a new departure, for it contains neither tropic acid nor tropine, but retains simply the form of an ester and the tertiary amino base. Here again the aim is to produce an antispasmodic drug acting on involuntary muscle and having no perceptible effects elsewhere. In fashioning these new compounds to produce particular effects, chemists start from the fact that the activity of atropine on the autonomic nervous system is centred in the tropic acid radical, and that the tropine base is practically inert. The essential reaction that they use is the esterification of tropic acid with a tertiary amino alcohol.

The atropine group of drugs are thought to act on the effector cells in the distribution of the cholinergic fibres of the autonomic system by blocking the acetylcholine effect; but it is by no means certain that the same mechanism accounts for their action on the brain. The contrast between the effects of atropine and hyoscine on cerebral function suggests that their pharmacological actions can hardly be identical. MEYERS and ABREU [1] have compared the central and peripheral effects of atropine, hyoscine, and some of the synthetic atropine-like compounds. They emphasise the importance of working on the living animal. In studies of the effects of the atropine group of compounds on the colon of the unanæsthetised monkey, they found that none of the synthetic drugs, except homatropine, compared with atropine in their ability to produce complete and sustained inhibition of motility of the large bowel. No-one would give these drugs by injection for their ocular effects, but it is of considerable academic importance that synthetic compounds which powerfully inhibit the alimentary canal were found to have a negligible effect on the pupillary reflexes. The action of these compounds on cerebration appeared to be biphasic, varying with the dose: small doses were apt to produce only lethargy; larger amounts were followed by hyperpnœa, excitement, motor weakness, and then drowsiness. MEYERS and ABREU claim that doses can be chosen which produce a persistent excitement, lasting for as long as forty minutes in the case of hyoscine and for a shorter time in the case of the synthetic drugs. They emphasise that "except for differences in potency as shown by the different dose required to produce the same effects no differences between atropine and scopolamine were observed." The subject is complex and is full of pitfalls for those who attempt its simplification. Although atropine and scopolamine are known to act in the same way on the peripheral autonomic nervous system, there are quantitative differences and peculiar contrasts in regard to the susceptibility of various tissues to the effect of the two drugs. On the heart, intestine, and bronchioles atropine has a much stronger and longer action; on the other hand, scopolamine is a more powerful blocking agent for the iris, ciliary body, and certain secreto-motor fibres (sweat, salivary, and bronchial glands). In clinical practice one complicating factor is the biphasic character of the response. This depends on the concentration of the drug in the tissues; and thus very small doses may evoke actions which are the very opposite of those following large doses. This biphasic response has been carefully studied by Dr. W. F. ANDERSON,[2] whose work is particularly important for its emphasis on the fact that tissue cells exposed to attack by powerful drugs may react differently according to whether they are, so to speak, suddenly overwhelmed by a high concentration of molecules or, on the other hand, given time to adapt to solitary invaders. As regards the atropine group, the biphasic response was observed by MEYERS and ABREU as an evanescent bradycardia, which they attributed to preliminary medullary stimulation; but usually this feature is likely to be obscured by the rapid onset of the drug's predominant action.

The newcomers among the atropine substitutes include 'Banthine,' which chemically resembles 'Panparnit' and 'Trasentin.' Here the objective seems to have been to evolve a more satisfactory drug for the treatment of diseases of the alimentary tract accompanied by spasm. CHAPMAN et al.[3] have carried out kymographic studies in healthy adults who had received 100 mg. of banthine. The effect was compared with that of tincture of belladonna; but it is noteworthy that the doses here were conservative—0·4 and 0·6 ml., equivalent to 0·12 mg. and 0·18 mg. of alkaloid. Banthine, it was found, caused a striking decrease in propulsive and total contractions and a slight to moderate decrease in tone. Banthine acted more rapidly and inhibited motility to a greater degree than did tincture of belladonna in either dosage. CHAPMAN et al. observed more dryness of the mouth after banthine than after tincture of belladonna, and also tachycardia—which did not occur in the tests with belladonna. This contrast in side-effects again raises doubt as to the adequacy of the doses of belladonna. Banthine was used by LEVY and ZWEIFLER [4] in 100 cases of infantile colic and vomiting. The result was classed as good in 68%, as moderately good in 12%, and as poor in 20%. It would be interesting to know what results might have been obtained from doses of belladonna large enough to produce minor side-effects.

1. Meyers, F. H., Abreu, B. E. *J. Pharmacol.* 1952, **104**, 387.
2. Anderson, W. F. *Lancet*, Aug. 9, 1952, p. 255.
3. Chapman, W. P., French, A. B., Hoffman, P. S., Jones, C. M. *New Engl. J. med.* 1952, **246**, 435.
4. Levy, H., Zweifler, B. M. *J. Pediat.* 1952, **40**, 570.

Annotations

DIURNAL EXCRETORY RHYTHM

SOON after birth a daily cycle of behaviour is established in relation to sleeping, waking, and feeding with subsidiary patterns of diurnal rhythm affecting other physiological functions. These include body-temperature, white blood-cell population in peripheral blood, carbohydrate metabolism, renal excretion of adrenocortical steroids, and renal excretion of water and electrolytes.

The excretory cycle of water and electrolytes has been known and investigated since 1877.[1] During the night there is a diminution in the renal excretion of water, sodium, potassium, chloride, and bicarbonate with a fall in urinary pH and a rise in urinary ammonia and titrable acidity.[2] In the morning there is an "alkaline tide" in the urine; this is unrelated to the gastric secretion of hydrochloric acid since it occurs despite achlorhydria or fasting. In addition there is a rising output of water and electrolytes, which reaches a peak about midday with a subsequent fall and a minimum output during the night. This complex cycle depends on fluctuations in renal tubular transfers of ions, since in the normal person there is little or no change in renal hæmodynamics (renal blood-flow and glomerular filtration-rate) or plasma-ion levels throughout the twenty-four hours.[3] While one might be tempted to ascribe the diurnal rhythm to a cycle of adrenocortical activity, as evidenced by diurnal variation of eosinophils in peripheral blood and of urinary excretion of adrenocortical hormones, the evidence is against this possibility.[4] The diminished pulmonary ventilation associated with sleep, and the resulting acidæmia, may be the factor determining the cycle of renal tubular function.[3] It is well known that, in acute experiments, hyperventilation and the resulting alkalæmia produce pronounced changes in renal ion clearances, though these are not quite comparable to the altered ion clearances brought about by waking.

Attention has lately been focused on the reversal of the diurnal rhythm of water and electrolyte excretion in congestive heart-failure accompanied by œdema and cirrhosis of the liver with ascites.[5] In such patients, however, it is noteworthy that there is an associated diurnal rhythm in renal hæmodynamics with maximum renal blood-flow and glomerular filtration-rate at night.[6] This may possibly be related to changes of posture or activity during the twenty-four hours. Such a renal hæmodynamics cycle, rather than an altered cycle in hormonal control of renal tubular ion transfers, may account for the reversal of diurnal rhythm of water and electrolyte excretion.

Our knowledge concerning the mechanism of the normal diurnal rhythm and its reversal in disease states is still incomplete. Will further research provide clues to that all-important problem—the unknown mechanism that controls the volume of extracellular fluid?

1. Quincke, H. *Arch. exp. Path. Pharm.* 1877, **7**, 115.
2. Stanbury, S. W., Thomson, A. E. *Clin. Sci.* 1951, **10**, 267.
3. Sirota, J. H., Baldwin, D. S., Villarreal, H. *J. clin. Invest.* 1950, **29**, 187.
4. Rosenbaum, J. D., Ferguson, B. C., Davis, R. K., Rossmeisl, E. C. *Ibid*, 1952, **31**, 507.
5. Jones, R. A., McDonald, G. O., Last, J. H. *Ibid*, p. 326.
6. Baldwin, D. S., Sirota, J. H., Villarreal, H. *Proc. Soc. exp. Biol., N.Y.* 1950, **74**, 578.

ADVANCES OF SCIENCE

SCIENTISTS must recall with sympathy the plight of that wrecked sailor who had so many things that he wanted to do that whenever he thought he would like to begin he couldn't, because of the state he was in. Luckily for us, or possibly unluckily, they have not stumbled on his masterly solution—which was to do nothing but basking until he was saved. Members of the British Association for the Advancement of Science, now meeting in Belfast, have so much to tell each other, and on such very different topics, that opportunities for basking must be strictly limited, despite the indulgent and excursive hospitality of their hosts, and the fact that the Mountains of Mourne are performing their well-known feat only a short drive away.

But, indeed, it is doubtful whether scientists are in the mood for basking. A hundred years ago their forerunners could carry their calling lightly, looking confidently forward to a benefited world. Today, as Prof. A. V. Hill, F.R.S., the president of the association, said of their ethical dilemma, "science finds itself unexpectedly and without those centuries of tradition and experience in a position no less important to the community than medicine: and its ethical principles have not yet clearly emerged." There seems, he concluded, to be no simple answer. Scientists are naturally as anxious about this as the rest of us; but they have accepted the duty of using their minds as well as they can to discover the nature of the universe, and like the rest of us they take refuge in their work.

Certainly they have plenty to occupy them. Their programme at Belfast contains no specifically medical section, but various sections touch on medicine—notably those on chemistry, zoology, physiology, psychology, and agriculture. Subjects of interest to doctors include such things as the control of the movements of the alimentary canal, the chemistry of bread-making, the assessment of personality, and Britain's food-supplies. In speaking of the problems of parthenogenesis, Prof. A. D. Peacock, D.SC., was not perhaps discussing a subject of immediate concern to us, but he raised some interesting speculations. In the last year, he recalled, G. Pincus and his associates have been responsible for the development of seven rabbit parthenogones; all were female, five were born alive, and one has since produced a litter of nine after normal mating. Pincus sees a possible application of the principle in stockbreeding: if cows could be made to breed females by parthenogenesis it would be extremely convenient.

VALVULOTOMY VERSUS SHUNT

CYANOTIC congenital heart-disease is nowadays treated surgically in centres all over the world as a result of the pioneer work of Blalock and Taussig[1] in Baltimore. Because these unfortunate patients can now be relieved, partly or completely, of their disabilities, interest has quickened greatly. The rapid advances in such techniques as cardiac catheterisation and cardioangiography have made it possible to reach an accurate preoperative diagnosis in almost every case; but there remains the question of which operation will afford the best result.

The shunt operation of Blalock is ideally suited to cases of severe pulmonary atresia or of tricuspid atresia. Pure stenosis of the pulmonary valves, however, clearly invites a more direct approach to widen the stenosed opening; and this Brock[2,3] has most successfully practised. The problem now before the cardiologist and cardiac surgeon (for it is imperative that they work together) is which patient will derive most benefit from a subclavian-pulmonary anastomosis, and which from a direct valvulotomy or infundibular resection[4] of the stenosed area. Pure pulmonary valvular stenosis (i.e., not associated with an interventricular septal defect) is best treated by Brock's direct attack on the stenosed opening with a valvulotome.[5,6] A Blalock shunt is contra-indicated since sooner or later right-sided heart-failure develops because the strain on the obstructed right ventricle is unrelieved. On the other hand, with atresia of the tricuspid valve so little blood enters the right ventricle that this is largely functionless, and pulmonary valvulotomy will be useless. In such patients

1. Blalock, A., Taussig, H. B. *J. Amer. med. Ass.* 1945, **128**, 189.
2. Brock, R. C. *Brit. med. J.* 1948, i, 1121.
3. Brock, R. C., Campbell, M. *Brit. Heart J.* 1950, **12**, 377.
4. Brock, R. C., Campbell, M. *Ibid*, p. 403.
5. Blalock, A., Kieffer, R. F. *Ann. Surg.* 1950, **132**, 496.
6. Potts, W. J., Gibson, S., Riker, W. L., Leininger, C. R. *J. Amer. med. Ass.* 1950, **144**, 8.

venous and arterial blood are mixed in the left ventricle and only an anastomosis between the systemic and pulmonary circulations—i.e., a Blalock or Potts operation—will allow the blood to enter the lungs and so relieve the cyanosis. Possibly there is one other group in whom a shunt type of operation must be carried out—those with such extensive pulmonary atresia that direct attack is impracticable.

Between these two groups of cases, in which the indications for either a shunt operation or valvulotomy are fairly precise, there lies a large number in which the decision may be difficult. Where a surgeon is more experienced in arterial anastomosis, he will naturally find himself treating most of his patients in this way. Others will favour the direct relief afforded by valvulotomy, and as they gain greater experience in its execution will find more cases to which it can be successfully applied. A recent report by Brock [7] is particularly illuminating. Of his first 223 cases of pulmonary stenosis, 112 were treated by anastomosis and 111 by direct operation; but in the first 50 there were 2 direct operations and 48 anastomoses, whereas in the last 50 there were 36 direct operations and only 14 anastomoses. Of these 14, 5 were cases in which a direct operation could not be done for reasons stated above.

The direct relief of pulmonary stenosis seems, therefore, to be technically possible in about two-thirds of the cases. It is certainly an attractive solution, since it largely restores to normal the mechanics of the heart, adds no new strain, and does not call for an artificial ductus with its potential risk of infection. Nevertheless only continued close study of patients treated by these alternative techniques will establish their relative values.

GETTING INTO STEP

THOSE of us who find irksome even the mild regimentation of contemporary civilian life will readily sympathise with the soldier who is "out of step." Usually he is a young man who finds that soldiering does not agree with him and that the consequences of kicking over the traces of discipline can be more unpleasant in the Army than in civil life. He may have wanted to be a driver, not an infantryman; if he could not be a driver he wanted to transfer to the Navy or the Mercantile Marine. He, and his like, find it hard to conform. They have not learned to swallow small injustices, and they almost inevitably run foul of the authority of the orderly room; and their "crimes" may range from personal neglect ("dirty rifle") to absence without leave. Sometimes their offences, though still not of a kind to get them into real trouble in civil life, are more serious and may vary from making Donald Duck noises on parade to throwing a bucket of whitewash over the regimental sergeant-major.

In 1941 the Army established at Pontefract a camp at which the training was to be "specially framed with a view to reclaiming young soldiers from a career of crime and converting them into good soldiers." Mr. Joseph Trenaman, who shared in the educational side of the venture, has described [8] the men who came to the camp, and how they fared there. Physically the men were weaker, feebler, and more ill-nourished than the ordinary run of young soldiers. They were a little below the average level in innate intelligence, but not obviously subnormal; emotionally they were immature. For the most part they came from poor and overcrowded homes. Only some 14% had been apprenticed to a skilled trade in civil life, and many had been in police trouble there; 36% had been convicted of indictable offences before joining the Army. But Trenaman believes that parental neglect was the "probable major factor" responsible for delinquency, with psychopathic states a poor second. Among the minor factors he lists, in order, physical deficiency, poverty at home, broken home, and invalid parents. Sir Cyril Burt, who contributes a stimulating preface to the book, does not like the term "psychopathic." It was a label bestowed by the psychiatrists who saw the men; but, as Burt says, different psychiatrists interpret the term in different ways.

Not all the men were enamoured of the new venture. It would have been overoptimistic to have expected otherwise. Some made it plain that they took a poor view of this latest outcropping of reforming zeal. The Glasgow youngster was probably not alone when he wrote across one of the early questionary forms, "none of your bissness." But the important thing is that the method seemed to bring results. The records of these lads were much better after treatment in the unit than they had been before.

ISOTOPES IN BRITAIN

DURING the late war British scientists heard with admiration—and not a little envy—of the remarkable developments in America as radioactive isotopes became available for biological research. These developments flowed directly from the brilliant work by American physicists in setting up cyclotrons and the first chain-reacting pile. After the war came a period when the United States with great generosity provided British workers with supplies of isotopes and information about the technique of their use in biological research. But these supplies were necessarily limited and could not in any case include the shorter-lived isotopes. It was therefore a great relief when the pile at Harwell came into action and home supplies were to be had. Now a wide range of isotopes can be obtained by British workers, and in addition Harwell carries on a thriving export trade.

With several years' experience now behind them, British workers can give a good account of themselves, as is shown by an issue of the *British Medical Bulletin* devoted to this subject.[1] A comprehensive review of this sort provides an opportunity for assessing the value of this fascinating and still novel application of physics to biology and medicine. The tale of what has so far been achieved has to be set against a background of the many technical problems that had to be overcome before any results at all were possible. Although nearly all isotopes are now prepared by neutron bombardment of suitable material in the pile, the actual production and isolation of each one involves an individual problem if material of the desired specific activity is to result. Isotopes are only useful to the biologist if they are present in the chemical form which he requires. For this reason the radiochemical centre at Amersham was set up. Here the necessary chemical manipulations can be carried out on highly radioactive substances; the compounds which the centre can supply include some forty labelled with C^{14}. In the subsequent handling of radioactive materials stringent precautions are needed, according to the type of radiation and the half-life of the isotope concerned.

In the measurement of radioactivity in tissues or whole organs there are many pitfalls for the unwary. The research-worker has to adjust himself to the new habits of thought required for the interpretation of experiments involving isotopes. He first has to become used to the idea that all his measurements are subject to an inevitable (but always calculable) error due to the random nature of atomic disintegrations, over and above any errors which may result from his manipulations. Then he must realise that his measurements only enable him to follow the fate of a small parcel of labelled atoms, introduced into his biological preparation at a particular time; rapid passage of a batch of labelled atoms through a given organ does not necessarily mean that large

7. Brock, R. C. *Ann. Surg.* 1952, **136**, 63.
8. Out of Step. JOSEPH TRENAMAN. London: Methuen. 1952. Pp. 223. 21*s*.

1. *Brit. med. Bull.* 1952, **8**, no. 2–3.

quantities of the corresponding unlabelled substance are passing through that organ all the time. A small sample of raw material may pass rapidly through a factory and be converted into the finished product; but if raw material is scarce the factory's total output may be low. Again, compounds neatly labelled by the introduction of a radioactive atom may be introduced into the body; but it cannot be assumed that the label will remain permanently in place. Finally a careful watch must be kept on the radiation received by the tissue under study, lest radiation damage should vitiate the result.

The technical and intellectual difficulties involved in work with isotopes are formidable: the compensating advantages are equally great. Where conventional chemical methods are too inaccurate or too laborious, or insufficiently delicate, isotopes often make possible an estimation that could not otherwise be effected. Studies on the metabolism of penicillin and vitamin B_{12} (described by E. Lester Smith) and on antigen-antibody reactions (A. Wormall) are good examples. Isotopes are particularly useful (as A. Neuberger shows for various proteins) in determining the average length of stay of the various component parts of large molecules incorporated in animal tissues. Then again, isotopes can be used efficiently in combination with another modern technique—paper chromatography. Gross and Pitt-Rivers demonstrate this elegant method in identifying a new iodine-containing compound in the blood of patients treated with radio-iodine.[2]

Thus isotopes make possible a new and more refined biochemistry, which is already reaping its harvest in many other fields. They can be used, for example, in clinical investigation, as C. H. Gray shows in his review on porphyria. But isotopes do not merely replace or extend chemical tests. They can be used, for instance, to label red blood-cells as well as molecules, and thus facilitate the estimation of blood-volume (E. B. Reeve). They can be used in conjunction with histology to show the location of elements within tissues (S. R. Pelc and A. Howard). Perhaps the most striking departure from traditional methods is in the detection and measurement of γ-emitting isotopes by external counters. Measurement of thyroid function in this way (described by N. B. Myant) may become a routine clinical test for thyrotoxicosis. The rate of disappearance of radiosodium, or its appearance elsewhere, after injection into the tissues or blood-stream, can give valuable information about rates of movement of ions into and within the blood (H. Payling Wright, E. M. McGirr) and even about the viability of the plastic surgeon's skin grafts (J. N. Barron and N. Veall).

Therapeutically, isotopes have great possibilities in the destruction of unwanted tissue. If that tissue is presented with a radioactive substance which it specifically concentrates, it can be bombarded from within, without risk to other tissues. Unfortunately this condition is still fulfilled in only a few instances. The thyroid gland is the clearest example. As E. J. Wayne and others show, thyrotoxicosis can be successfully treated with radio-iodine. The same is true of those thyroid cancers which concentrate iodine, though the differential concentration is nothing like as great as in thyrotoxicosis, and therapeutic bombardment is consequently more difficult to achieve (R. Paterson and others). The presentation to cancerous tissue in general of an effective isotope in a chemical form which would be concentrated specifically is very much in the minds of those working on the subject, but its achievement is not yet in sight. For the present we must be content with bringing the radioactive material into as close contact as possible with the tissue which needs to be destroyed. This has been done with some success in the case of bladder tumours by introducing balloons containing solutions of radioactive sodium or bromine (R. J. Walton and W. K. Sinclair). Some relief can be achieved in malignant pleural and peritoneal effusions by partial replacement of the fluid with suspensions of colloidal radio-gold.

In summary, the isotope technique has already made major contributions to fundamental biology. It is proving useful in clinical investigation and has had sufficient therapeutic success to justify hopes of better things to come. Owing to the technical complexities and health hazards, the handling of isotopes is best left to research-workers for the time being. But it is well that the rest of the profession should know what is going on in this field, for the potentialities of the method are so great that its applications might, in the future, be the concern of us all.

2. See Gross, J., Pitt-Rivers, R. *Lancet*, 1951, ii, 766; *Ibid*, 1952, i, 439, 593. Gross, J., Pitt-Rivers, R., Trotter, W. R. *Ibid*, p. 1044.

STREPTOCOCCI AND RHEUMATISM

THE generally accepted view that recent streptococcal infection is the underlying bacterial cause of acute rheumatism leaves unexplained many of the baffling problems in this group of diseases. Clinically acute rheumatic fever resembles serum sickness quite closely, and many workers have suggested that the clinical features of rheumatic fever are due to an antigen-antibody reaction at special situations in the body.[1] This hypothesis has been too vague to carry us very far. Many different kinds of antigen have been tested, ranging from streptococcal "toxins" to hypothetical antigens from the patient's own tissues; and lesions resembling those of rheumatism have been produced by various experimental procedures. But there is still no really convincing explanation of the specificity of the lesions or the relative parts played by the streptococcus and the patient's own tissues in determining this specificity.

Dr. Glynn and Dr. Holborow have investigated these problems in some new experiments, which they describe in this issue. It is now recognised that the specificity of a protein can be profoundly modified by chemical combination with non-protein substances known as haptens. By suitable combination of a bacterial protein with, for example, a polysaccharide, a new antigen can be created which has the specificity, not of the original protein, but of the polysaccharide which has been attached to the protein. Glynn and Holborow, using β-hæmolytic streptococci (group A, type 4) as source of bacterial "protein" and a solution of chondroitin sulphate from human costal cartilage as polysaccharide, prepared a chondroitin sulphate streptococcus vaccine. Rabbits received intravenous injections of this vaccine, a control vaccine of the same streptococcus not treated with chondroitin sulphate, and a solution of the chondroitin sulphate alone. Five out of six rabbits which received the chondroitin sulphate streptococcus vaccine showed evidence of joint lesions—some with acute synovitis—and the serum of all these animals gave a positive precipitin reaction with chondroitin sulphate solution. Control rabbits that received either the streptococcal vaccine or the chondroitin sulphate alone showed no comparable joint lesions, and neither these nor normal rabbits showed any precipitin reaction with chondroitin sulphate.

The combination postulated by Glynn and Holborow may possibly occur in a slightly different way: instead of the streptococcus providing the protein and the patient's tissues the hapten, the rôles may conceivably be reversed and the streptococcus provide a hapten which converts tissue proteins into "auto-antigens" with a new specificity. There is some experimental support for this concept. For example, Goebel and Avery[2] showed that a pneumococcal polysaccharide which acts only as a hapten when injected into rabbits can be made fully

1. See Fischel, E. E. *Amer. J. Med.* 1949, **7**, 772.
2. Goebel, W. F., Avery, O. T. *J. exp. Med.* 1931, **54**, 431. Avery, O. T., Goebel, W. F. *Ibid*, p. 437; *Ibid*, 1938, **58**, 731.

antigenic by conjugating it artificially with a suitable protein, whereas a pneumococcal polysaccharide which is non-antigenic when injected into rabbits is fully antigenic by itself in mice and men.

The discovery of the dramatic effects of adrenocorticotropic hormone has given a new impetus to the study of the rheumatic diseases; and the possible interrelation of hormonal factors, of the allergic state, and of an extrinsic bacterial agent poses some intriguing questions. The experiments described by Glynn and Holborow are interesting and suggestive; and we hope that these will be followed by further work on similar lines.

SEX-HORMONE METABOLISM IN LIVER DISEASE

CERTAIN clinical manifestations of liver disease have been thought to result from altered intrahepatic metabolism of steroid hormones with consequent disturbance of the normal balance between œstrogens and androgens.[1] In the male the most important clinical features of this sort are gynæcomastia, testicular atrophy, and loss of libido. Cutaneous spider nævi, palmar erythema, and loss of hair on the chest have also been attributed to a similar mechanism. Experimental data leave little doubt that the liver plays an important part in inactivating œstrogen; and observations in the rat have shown convincingly that this function may be impaired by malnutrition.[1] On the other hand, it now seems doubtful whether these results apply to other species. Zondek and Brzezinski,[2] for example, found that inactivation of œstrone was unimpaired in women with severe vitamin-B deficiency, while Hooker et al.[3] found that in primates the result of intrasplenic implantation[4] was the same as with administration by any other route. Direct evidence of hepatic inactivation in man has, however, now been described by Evans et al.[5] 9 patients receiving œstrogen therapy for carcinoma of breast or prostate were chosen because of their high blood-œstrogen levels. These levels were determined in samples taken simultaneously from the hepatic vein and the femoral artery. In 6 cases evidence of significant inactivation by the liver was detected. In the 3 cases where inactivation was insignificant the patients were severely undernourished.

Several attempts have been made to establish by assay of the hormones in the urine that such conditions as gynæcomastia arising in chronic liver disease result from impaired hormone metabolism. Rupp and his colleagues[6] found an increase of urinary œstrogen in 16 out of 25 cases of hepatic disease with gynæcomastia, but the over-all correlation was poor. Dohan et al.[7] also found no apparent correlation between the severity of the hepatic disease and gynæcomastia, or between gynæcomastia and the absolute values of urinary œstrogens. A further study of this problem by Dohan and his colleagues[8] provides, however, a possible explanation of such inconclusive results. 17 men with diffuse liver disease and 5 normal controls were included in this study. The severity of the disease was assessed by clinical examination, liver-function tests, and biopsy specimens. Hormone excretion was estimated on specimens of urine collected over several days, to minimise errors due to daily fluctuation; the estimations included the free and conjugated forms of œstradiol, œstrone and œstriol, and gonadotropin, all by biological assay, while total neutral 17-ketosteroids were estimated by a colorimetric method. Increased excretion of total œstrogen and decreased output of ketosteroids and gonadotropin was found to run approximately parallel with the severity of the disease. Urinary œstrogen was significantly correlated only with the serum-bilirubin and bromsulphalein retention—i.e., with tests of excretory function. Presumably the decreased ability of the diseased liver to excrete œstrogens accounts for the increased output by the kidney. The liver's ability to conjugate the steroids with glycuronic acid is apparently unaffected, since the increase of the combined form of the hormones in the urine is usually far greater than that of the free forms. The total œstrogen excretion, and still more the œstrogen-ketosteroid ratio in the urine, were significantly greater in the four cases with stable gynæcomastia than in those with regressing breast changes or no such changes at all. Dohan and his colleagues emphasise the importance of differentiating cases with persistent gynæcomastia from those in which the breast changes are reverting to normal, and suggest that failure to mark this distinction is the cause of previous failure to establish the relationship between the breast enlargement and the level of circulatory hormone as assessed by urinary excretion. The only test that could be correlated with spider nævi was that of free œstriol excretion; but a highly significant relationship was found between testicular atrophy with loss of libido and decreased excretion of gonadotropin.

These results confirm what has long been suspected, both on clinical grounds and from experimental work—that hormonal imbalance may result from impaired metabolism of hormones by the diseased liver. Excess of œstrogens is the most conspicuous result; but androgens may also be affected—a disturbance indicated by impotence associated with a fall in ketosteroid excretion due, at least partly, to diminished secretion of gonadotropin by the pituitary.

DEATH AFTER INOCULATION

MAINLY as the result of mass immunisation, begun in 1940, the extinction of diphtheria is in sight; and whooping-cough is now the most formidable acute specific respiratory disease of infants and very young children. A similar campaign against this disease, although long delayed by the need for large-scale controlled trials of vaccines made from numerous strains of *Hæmophilus pertussis* by different techniques,[1] is now in progress, and many thousands of children have already been inoculated without untoward effect other than an occasional transient local or general reaction caused by sensitivity to proteins of the dead organisms from which the vaccine is prepared. It is therefore disconcerting to learn of an inquest on a 2-year-old child who developed an abscess in the right upper arm after a second prophylactic injection of a whooping-cough vaccine and who later died of septicæmia—a sequel unique in the experience of the medical witnesses.[2] Since eight other children were inoculated with the same batch of vaccine, apparently without ill effect, the vaccine itself is clearly exonerated. Anyhow the tests for sterility by the manufacturers of this and other biological products for injection are so stringent that contamination of the contents of an ampoule before it is opened is extremely unlikely. At the inquest a pathologist expressed the opinion that death resulted from an accidental skin infection. Nevertheless, this tragedy should cause all who have to give parenteral injections to look to their technique.[3] The potential danger of infection of the needle-puncture from pyococcal skin lesions should also be borne in mind; and if such lesions are detected, prophylactic injections should be postponed.

1. Leading article, *Lancet*, 1952, i, 350.
2. Zondek, B., Brzezinski, A. *J. Obstet. Gynec.* 1948, **55**, 273.
3. Hooker, C. W., Drill, V. A., Pfeiffer, C. A. *Proc. Soc. exp. Biol., N.Y.* 1947, **65**, 192.
4. Biskind, M. S. *Vitam. & Horm.* 1946, **4**, 147.
5. Evans, J. M., Young, J. P., Hertz, R., Tullner, W. W., Wilmer, G., Wood, O. *J. clin. Endocrinol.* 1952, **12**, 495.
6. Rupp, J., Cantarow, A., Rakoff, A. E., Paschkis, K. E. *Ibid*, 1951, **11**, 688.
7. Dohan, F. C., Richardson, E. M., Bluemle, L., Gyorgy, P. *J. clin. Invest.* 1950, **29**, 808.
8. Dohan, F. C., Richardson, E. M., Bluemle, E. W. jun., Gyorgy, P. *Ibid*, 1952, **31**, 481.

1. Medical Research Council. *Brit. med. J.* 1951, i, 1463.
2. *Evening Standard*, Aug. 27.
3. See Parish, H. J. Bacterial and Virus Diseases. Edinburgh, 1951. Sterilization, Use and Care of Syringes: Medical Research Council War Memorandum no. 15. H.M. Stationery Office. 1945.

Public Health

THE NEED FOR AN OCCUPATIONAL HYGIENE SERVICE

PETER H. NASH
M.A., M.D. Camb., D.P.H.

SENIOR CLINICAL ASSISTANT, SLOUGH INDUSTRIAL HEALTH SERVICE; LECTURER IN INDUSTRIAL PHYSIOLOGY, LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

OCCUPATIONAL hygiene is the measurement of the industrial environment and its effects on workers' health. Though the advantages of this approach to industrial health problems have been appreciated in this country for many years, almost nothing has been done to apply it on a large scale. In the development of our industrial health services the emphasis has been on factory inspection—largely from a safety point of view—on the one hand, and health care by industrial medical officers on the other. In these aspects of occupational health, and also in factory legislation and notification of occupational disease, we have been pioneers and still have probably the finest services in existence. Unfortunately this is not true of our occupational hygiene facilities. Indeed no service of this kind exists and our country lags behind others.

AMERICAN PRACTICE

In the United States industrial health services developed rather differently. The great increase of production during the first world war resulted, as here, in outbreaks of industrial disease. To combat these, individual States set up divisions of industrial (or occupational) hygiene, usually as a branch of the State public-health department. These developed greatly between the two wars and now most States, and even some cities, have such divisions. They are based on a laboratory where physicians, engineers, chemists, and industrial nurses work together on occupational health problems. Each specialist lends his particular skill to the task. For example, a visiting factory inspector or nurse may be the first to discover a possible toxic hazard. The physician may then visit the factory and, by studying the environment, talking with management and workers, and making clinical and laboratory examinations of those likely to be affected, decide whether a health hazard exists. Chemists and engineers then survey the factory, taking air-samples in different parts, and measure the amount of toxic substance present in the air. If a health hazard is discovered the correct preventive action can be determined in the light of the known facts. In this the engineer, with his special knowledge of exhaust ventilation and other protective devices, plays a large part.

These laboratories carry a full range of equipment for assessing most physical hazards in industry. Thus they are able to analyse air and body-fluids for toxic substances, to perform dust-counts and analyses, measure radiation, and conduct lighting and thermal comfort surveys. An important point is that they are not organised for research, though research is of course done. Their main work is to help and advise industry in health. Much of the work is routine—for instance, repeated examinations in lead-works of air-samples, and urine and blood specimens. In this country there are no facilities for regular surveys of this kind, apart from blood-counts, except where the firms provide them. The occupational hygiene division also acts as an advisory centre on all matters of occupational health. Help is given to firms which wish to start their own medical services, and there is often an industrial nursing consultant who acts as focal point and adviser to all industrial nurses in the area.

Many other countries have developed such services—e.g., Canada, Finland, Peru, the Philippines, Sweden, the U.S.S.R., and Yugoslavia.

A FIRST STEP

I believe that there is a real need for a service of this kind. Anyone with access to a large number of factories, as we have at Slough, must come to realise that there is a great deal of occupational ill health which is never recognised, let alone notified. Through ignorance dangerous solvents and other toxic substances are used carelessly, and may cause disease which long remains undiagnosed. Men are also often exposed to high concentrations of the less dangerous solvents, and minor health impairments or worry over the effect of the fumes may lead to loss of production. Fettlers and grinders may work in confined spaces with high dust-concentration, their only protection a calico mask which they are expected to wear continuously. Often lighting, heating, or ventilation is poor, and recurrent though preventable eye injuries are found.

These situations arise because managements of small firms are not in a position to obtain advice on health matters. When advice is given in convincing form, they are usually anxious to coöperate and improve working conditions. A detailed survey of conditions, from medical and engineering aspects, figures for air-concentrations, and suggestions for action are far more effective in producing a positive response from management than mere verbal arguments.

The Factory Department of the Ministry of Labour and National Service has 16 medical inspectors of factories who are responsible for the whole of England, Scotland, and Wales. These inspectors have a wider knowledge of occupational hygiene than anyone else in the country, yet they have no technical assistants and no suitable laboratory behind them. Samples for analysis are sent to the Government Laboratory and, because only occasional samples can be analysed, few, if any, complete and repeated occupational hygiene surveys can be made. The situation would be very different could there be many more medical inspectors and regional laboratories, with engineers and chemists, to help them. The Medical Research Council's Unit for Research in Industrial Medicine has a fine laboratory and is able to undertake any kind of factory survey, clinical or environmental. It, however, exists primarily for research—and rightly so—and cannot carry out routine work or cope with the many small problems that exist up and down the country. Really serious hazards—such as instances of beryllium poisoning or the recent outbreaks of poisoning by dinitro-*ortho*-cresol—are dealt with immediately and effectively, yet the multitude of smaller problems cause greater loss of health and production.

Realising the need for this preventive approach to occupational health, the Nuffield Foundation and those working at Slough were responsible, in 1949, for sending an engineer, Mr. R. J. Sherwood, to Harvard to be trained in occupational hygiene techniques. After his return a small team was formed, consisting of myself as physician, Mr. Sherwood as engineer, and Miss Joan Bedford as chemist, to investigate occupational health problems at Slough and elsewhere. The foundation made a grant towards an occupational hygiene laboratory which has been set up at the London School of Hygiene and Tropical Medicine. Samples collected in the field are brought to this laboratory for analysis, counting, and so on. The laboratory is part of the occupational health sub-unit which also plays a part in teaching students of the D.P.H. (industrial elective) course and public-health engineers.

The number of requests for help which we have received has been greater than so small a unit can cope with. As well as the regular work at Slough on the discovery and control of toxic hazards, skin irritants, and uncomfortable working conditions, there have been requests for advice from managements who were about to instal new processes or who wished to check safeguards

which they had installed. We have also had many calls for advice from industrial medical officers or direct from managements of firms in all parts of the country. Our experience has convinced us of the need for a service which can give technical help to industrial medical officers and, even more, to firms with no medical care. An occupational hygiene service to cover the entire country would need perhaps six or eight units, staffed with doctors, engineers, chemists, and physicists. If any industrial health service was later set up these centres could form an integral part of it.

A NATIONAL SERVICE

A precedent for these centres already exists in the Public Health Laboratory Service, which is administered by the Medical Research Council. There are 18 special or reference laboratories and a further 49 constituent laboratories in different parts of the country. Nothing like this number of occupational hygiene centres would be needed, but their administration by the Medical Research Council for the Ministry of Health following the pattern of the P.H.L.S. is a possibility.

There is also a strong case for the centres to become part of the Factory Department of the Ministry of Labour and National Service. This department has the necessary experience and a corps of medical inspectors who could act as leaders of the project. Further, the work of the service would be largely inspection, using every available scientific means, rather than research.

Another possibility is that industry itself should be encouraged to set up these centres. The National Coal Board, for instance, is already doing, and planning to do, preventive work based on research carried out by the Pneumoconiosis Research Unit of the Medical Research Council. The Industrial Hygiene Research Laboratory of Imperial Chemical Industries is an example of what a single large firm can do. Other large firms might do the same, but in many the hazards are not numerous enough to warrant such provision. Some industrial organisations, such as the Shirley Institute (cotton), the British Cast Iron Reserach Association, and the British Iron and Steel Research Association, already carry out some occupational hygiene investigations, though they are not primarily interested in health. Some of them are associated with the Department of Scientific and Industrial Research, which suggests the possibility of a combined private enterprise and Governmental approach.

Finally, some universities might consider it of value, from the point of view of teaching, to join in work of this kind, perhaps in coöperation with another agency such as the Factory Department. But whatever the form of organisation chosen, it is important that something should be started now. The health of our workers and the output of our factories should no longer be allowed to suffer for want of reasonable facilities in occupational hygiene.

I should like to place on record the names of those who foresaw the need for occupational hygiene at Slough and elsewhere in this country, and were responsible for sending the first engineer to train under Prof. Philip Drinker at the Harvard School of Public Health. They are Dr. A. Austin Eagger, Prof. J. M. Mackintosh, and Dr. M. E. M. Herford.

Poliomyelitis

In the week ended Aug. 23 notifications (uncorrected) of poliomyelitis in England and Wales were as follows (figures for the previous week in parentheses): paralytic 152 (170); non-paralytic 68 (88); total 220 (258). This brings the total for the 34 weeks since the start of the year to 2388, compared with the following totals for the same period in each of the five previous years: 1951, 1747; 1950, 4125; 1949, 2033; 1948, 1067; 1947, 3619.

According to the Weekly Epidemiological Record, issued by the World Health Organisation, there has been a definite recrudescence of the disease in Europe, and notably in parts of Western Germany, the Netherlands, and Belgium. In the U.S.A.[1] 2648 cases were reported during the week ended Aug. 9; this was an increase of 15% over the figure for the previous week. Up to Aug. 9 the cumulative total for the "disease year," which began with the week ended April 5, was 12,046; the corresponding figure last year was 7056. The incidence has also been increasing in Canada, particularly in the west, where quarantine restrictions have been imposed at two large military stations, from one of which 17 cases had been reported.[2]

International Certificates of Vaccination

The International Sanitary Regulations adopted by the Fourth World Health Assembly come into force on Oct. 1. New and simpler forms of certificates of vaccination against smallpox and cholera will then be used.

Persons going abroad, who are vaccinated against these diseases *after* that date, should have their certificates on the new forms, obtainable from the company arranging their passage. International certificates for vaccination done *before* that date remain valid for the period shown on them.

The international certificate of vaccination against typhus has been abandoned, because this vaccination is no longer required internationally.

Medicine and the Law

Murder and Abnormality

THERE is notoriously an unbridged gulf between the forensic and the medical view of insanity in relation to criminal responsibility. Two recent cases in the Court of Criminal Appeal show afresh how far the two are apart.

On the appeal of J. H. Godar,[1] convicted of murdering Maureen Cox, his counsel, Mr. G. D. Roberts, Q.C., conceded that at the trial the summing up had been full and fair and that there had been evidence on which the jury could properly find a verdict of guilty; in other words there were no grounds for an appeal. It appeared that Godar had in 1944, while serving in the Army, been found to be suffering from a disease of the mind amounting to defect of reason. This fact, however, was not mentioned as a matter for the appellate tribunal to consider; it was merely referred to by counsel, in passing, as one which the Home Secretary might perhaps take into account when advising the Crown as to the exercise of the prerogative of mercy.

On the other appeal, that of J. T. Straffen,[2] the apparent irrelevance of the appellant's mentality was even more striking. At his trial there had been evidence of his having been certified a mental defective, of his having formerly been found unfit to plead to a criminal charge, and of his having strangled two other little girls in addition to the 5-year-old Linda Bowyer whom he was accused of having murdered.[3] The Court of Criminal Appeal was not asked to note his obvious abnormality; it was irrelevant; the two grounds of appeal (technical questions of the admissibility of evidence, legally, no doubt, of great importance) ignored it. Even had the case found its way up to the House of Lords, his mental condition would still doubtless have been immaterial. Public opinion, as well as medical science, may be convinced of the irresponsibility of men like Straffen. The criminal law goes on its majestic way unconcerned.

"There are," wrote the late Sir Edward Troup, a former head of the Home Office, "a certain number of borderline cases in which the question whether a prisoner is insane,

1. Morbidity and Mortality: Weekly report by the Federal Security Agency, Public Health Service. Washington, D.C., Aug. 15, 1952.
2. *Times*, Aug. 29.
3. *Ibid.*, Aug. 20.
4. *Ibid*, Aug. 21.
5. *Lancet*, Aug. 2, 1952, p. 239.

though negatived by the jury or not raised at the trial, has to be considered after conviction." If medical experts then certify the prisoner insane, "there is a consensus of legal authority for the view that it would be contrary to the common law to allow the execution, and the records which go back to 1840 show no exception to this rule." Accordingly on the advice of his panel of doctors the Home Secretary has recommended that Straffen should be reprieved. Thus, in the end, the medical opinion prevails over the judicial sentence after all. Sir Edward went on to give statistics showing that, over the 22 years from 1901 to 1922, out of 585 persons convicted of murder 517 were found to be insane, either before trial or by special verdict of the jury or on Home Office inquiry after conviction. If, as is probable, more recent totals show a not dissimilar proportion, is it not time for another review of insanity in relation to crime such as that which the Atkin Committee conducted thirty years ago? As Sir Russell Brain, P.R.C.P., has pointed out[6] the circumstances in which mental illness should mitigate criminal responsibility "is a question, not for lawyers or doctors, but for society to decide"; and he, too, thinks the question should be reconsidered, perhaps by a Royal Commission.

6. *Times*, Sept. 1.

Points of View

CURE OF TOBACCO-SMOKING

LENNOX JOHNSTON
M.B. Glasg.

"How can I stop smoking?" I, who stopped many years ago, have often been asked. "By not smoking again," is the brutal correct answer; for every movement of smoking is voluntary. "But I have tried repeatedly and failed; I haven't enough will-power. Is there a way in which I can be helped to stop?" "Yes, there is a way," is the answer; and the purpose of this article is to show it.

The view that smoking can be stopped only by the exercise of will-power is almost universally accepted. Yet it is only part of the truth. For "knowledge is power" (or will-power) when acted upon. The greater the volume and more impressive the character of knowledge, the more insistently does it demand effective expression (in action). When knowledge is repressed, or is merely expressed in words unsupported by actions (when, for example, a smoker says, "I *know* that smoking is harmful" but continues to smoke), the power of knowledge is insufficient (usually because of insufficiency of knowledge) to compel its effective expression.

The urge to smoke is at first purely psychological—a desire. While it remains so, it is easy to give up smoking. As smoking proceeds, however, the urge becomes increasingly compulsive: the psychological urge has been reinforced by a pharmacological urge, the craving for tobacco.

PSYCHOLOGICAL URGES TO SMOKE

The desire to smoke originates from the advocacy of smoking by smokers, much of it unconscious. Each time a smoker lights up, he says in effect, "I am in favour of the smoking of tobacco, I approve of smoking"; and little weight attaches to any mere words he may utter in contradiction to his actions. Each proferred cigarette, each word of approval of smoking, written or verbal, is smoking propaganda. Every smoker is, in fact, whether he wills it or not, a living advertisement for tobacco, and there are so many smokers today, and they smoke and speak encouragement to smoke so often, that the persuasive pressure on non-smokers to commence or recommence smoking is powerful indeed. To this must be added the lavish scientific advertising of the tobacco combines. In the United States of America in 1945 it was calculated that almost 3000 non-smokers start to smoke every day.[1]

The initial desire to smoke is closely associated as a rule with one to appear grown-up or sophisticated, to imitate someone admired—usually Daddy or, nowadays, Mummy—or to be companionable or sociable. Later there is a recurring desire to perform the now largely habitual and often ritualistic actions of smoking, particularly at certain times—e.g., after meals—or to relieve boredom or nervousness. Freud drew attention to the possibility that oral-libidinal satisfaction—the association of smoking with the infantile pleasure of suckling—may also urge people to smoke.[2]

Psychological "infection" of the non-smoker is completed, as a rule, by the intimate persuasion of a smoker: "have a cigarette, old man"; "it'll do you good (or steady your nerves)"; "don't be so miserable (or a cissy)"; "one has to have a bit of pleasure (or comfort) these days"; or "one has to have one little vice; it doesn't do to be too good." Besides simple persuasion, reinforced by example and free samples, smokers use—though as a rule without realising it—less ethical methods of infecting non-smokers. Thus they suppress the facts, particularly the more damning facts, against smoking, and circulate in their place favourable untruths: in short, they use deception.

PHARMACOLOGICAL URGES TO SMOKE

Having established, on myself and 35 volunteers, that the repeated administration of nicotine is a satisfactory substitute for tobacco-smoking,[3] I decided to ascertain how long craving for a drug of addiction takes to develop.

I was at that time somewhat addicted to nicotine, so I had to use another drug. I gave myself hypodermically, night and morning, cocaine hydrochloride, a drug I had not taken previously, in doses ranging from $^1/_4$ to 1 grain (16–64 mg.). About 5 min. after administering each dose, I experienced a curious sensation which I find impossible to describe: it was readily distinguishable from nicotine and codeine (whose actions are equally indescribable), but was not pleasurable. This occasioned me and a control volunteer to whom I administered several doses, some surprise—and, indeed, disappointment, for we had recently had considerable pleasure from experimental doses of nicotine. About 10 days after commencing the administration of cocaine, I found myself looking forward to the next dose with considerable satisfaction, and after 25 doses deemed it advisable to discontinue the experiment lest I became strongly addicted.

The slight craving I had acquired lasted several days, and could readily be recalled in fantasy for a much longer period. It must have developed as a side action of cocaine, and been built up cumulatively. With the craving came pleasure on its appeasement; and it seems clear that the pleasure derived from drugs of addiction arises mainly from the appeasement of craving, once such craving has been acquired. Pharmacological craving is clearly a specific, abnormal appetite for a drug, hostile (because of the drug's toxicity) to the normal, though not to the abnormal, functioning of the organism. Its development completes a vicious circle: administration gives rise, though not immediately, to craving, which leads to further administration. Once set in motion, this circle continues to turn without, as a rule, interference from the smoker's will.

Besides appeasing the craving of addicts, drugs of addiction have a further immediate specific pharma-

1. Clean Air. No. 39. April–June, 1948, p. 4.
2. Freud, S. Three Essays on the Theory of Sexuality. Translated by James Strachey. 1949; p. 61.
3. Johnston, L. *Lancet*, 1942, ii, 742.

cological action on both addicts and non-addicts. Smokers do not enjoy the pharmacological action of tobacco smoke at first—indeed, they usually dislike it. But as time goes on they find that, besides deriving positive pleasure from the appeasement of their craving, they have, if they be inhalers, an almost instantaneous general analgesic against life's little, or even big, stresses and vexations. The inhalation of cigarette smoke in moments of severe stress, in fact, is reminiscent of the inhalation of gas-and-air by a woman in labour. In pipe-smoking, the analgesic (or sedative) effect is delayed for about 10 minutes, since the absorption of nicotine is mainly alimentary. Unfortunately, the pleasurable analgesic action of nicotine (and of other drugs of addiction) is more than offset by after-depression and apathy. This cannot, of course, be demonstrated, since changes in mood are subjective; but I have observed that a striking and sustained uplift of spirits and of general interest almost invariably accompanies the giving up of smoking; and that heavy smokers seem as a class more depressed ("fed up") than non-smokers.

The effects of the psychological and pharmacological urges cannot be separately demonstrated, nor can their relative strengths be measured; only their combined effect on conduct is obvious. But interrogation of (I estimate) about 10,000 cured smokers over the past 24 years, and a personal analysis based on stopping smoking four times (twice experimentally), and on taking some 200 doses of nicotine by various routes, have convinced me that the pharmacological craving for tobacco though strongly compulsive, at first, is short-lived, at any rate in its acute form. It reaches its peak 24–36 hours after smoking has been stopped and thereafter sharply and steadily declines, though the initial steepness of the decline is not maintained: it takes several months, indeed, to reach zero.

Psychological urges to smoke, on the other hand, do not decline steadily when smoking is stopped, since most of the psychological stimuli which produce them persist. In my case, the desire for the general analgesic action of nicotine persisted, in times of particular stress, for more than a decade; so also did the less compulsive urge to smoke for companionable reasons. The desire for a plaything—the wish to perform the habitual actions of smoking—scarcely troubled me, and could in any case have been almost completely satisfied by performing the actions of smoking without actually lighting the cigarette. The longing of the recently cured smoker, after a meal, is not to perform the habitual actions of smoking, but to administer his postprandial dose of nicotine.

If, after he has smoked for some time, the smoker loses desire to smoke, and wishes to stop smoking, a conflict develops between opposing urges—the will to stop smoking, on the one hand, and craving for tobacco reinforced by various psychological urges, on the other. If the smoker's will prevails, smoking is cured temporarily or permanently. If, however, his involuntary urges prevail, he continues to smoke; but his smoking no longer expresses his will. He therefore tends to repress the whole conflict, for the outcome has been damaging to his self-esteem. He attributes his smoking solely to socially approved urges such as habit, the relief of boredom, or a simple desire for enjoyment. Smokers who have tried unsuccessfully to stop smoking, though they seldom realise or admit it, are unwilling smokers.

All smokers, willing and unwilling, however, encourage the spread of smoking and add to tobacco consumption. This has risen in Great Britain from 166 million lb. in 1913, costing £8,300,000, to 281 million lb. in 1948, costing £42,800,000. The increase in smoking has resulted in the progressive elimination of one non-smokers' sanctuary after another—drawing-room, bedroom, workroom, place of entertainment, conveyance, and finally, of late years, hospital ward and sanatorium, even when and where patients seriously ill from respiratory diseases are under treatment. The problem of sanctuary for those who claim (as I do) that the right to breathe clean air—air free, at any rate, from irritant fumes—is as basic, in a civilised country, as the right to drink clean water, has become today almost insoluble even when they are ill.

HOW TO STOP SMOKING

It is difficult to stop smoking—very difficult indeed if one is a heavy smoker of long duration. In order to stop, it is necessary to do much more than merely decide. Intellectual conviction that smoking should be abandoned is an essential preliminary, of course, to stopping, but it is only a preliminary. There must also be a build-up of resolution sufficient to withstand indefinitely all urges to smoke. As in war, the more overwhelming the preparatory build-up of strength (or resolution), the easier and more certain the victory; and conversely, irresolution tends to prolong the struggle and jeopardise success. Resolution not to smoke is born, as already indicated, of a sound and clear, though not necessarily extensive, knowledge of the action of tobacco smoke on the human organism.

The most difficult task, as a rule, is to make the break—to withstand the first surge of craving. Half the battle is over when the first day and night of non-smoking are completed. It is best, in my experience, to stop suddenly, abruptly, completely, ignoring all symptoms which might possibly be associated with tobacco deprivation. Detoxication, and hence improvement in health, begin directly smoking is discontinued, no matter how the smoker may feel; so he must follow his purpose without regard to his feelings. All thoughts about smoking should be rigorously excluded from consciousness, because craving precludes, for a time, objective thinking on this subject. It may help if he treats the craving contemptuously from the start, by carrying for a time (while resolution runs high) the paraphernalia of smoking. The more inflexible the determination to end smoking, the less the pain: as in grasping nettles, pain varies inversely with firmness. It is well to proceed silently, unobtrusively: the raillery of smokers is shrewdly calculated to undermine resolution. Acute affections, particularly respiratory affections, temporarily remove or greatly reduce all urges to smoke. A good time to stop, therefore, is when such an affection develops; or respiratory inflammation may be produced artificially, to some extent, by smoking very heavily the night before.

Psychotherapy consists in building up the patient's determination to end smoking by persuasion, encouragement, undeception, and re-education—patient and oft repeated when necessary—until, in favourable cases, its expression in non-smoking becomes irresistible. Fear, particularly of lung cancer (though this is a long-term risk) can be a potent psychotherapeutic agent, and the use of such intimidation is clearly justified when—as in this case—it is based on fact, or at any rate strong probability. A first, often difficult, task is to dispel defeatism born of previous, sometimes repeated, failure—failure almost invariably associated with ignorance of essential facts about smoking. Friends ought perhaps to be warned against irritability; but I believe I displayed none, and I suspect that it may in some cases be "laid on" by the smoker in the hope of getting his wife or fiancée to entreat him to recommence smoking, and thus shoulder some of the blame for relapse.

Unless psychotherapy has been extremely thorough, there is great risk, with so much psychological infection about, of relapse, particularly at times of lowered resistance—e.g., on sociable occasions, or in moments of stress. To avoid this,

Public Health

THE NEED FOR AN OCCUPATIONAL HYGIENE SERVICE

PETER H. NASH
M.A., M.D. Camb., D.P.H.
SENIOR CLINICAL ASSISTANT, SLOUGH INDUSTRIAL HEALTH SERVICE; LECTURER IN INDUSTRIAL PHYSIOLOGY, LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

OCCUPATIONAL hygiene is the measurement of the industrial environment and its effects on workers' health. Though the advantages of this approach to industrial health problems have been appreciated in this country for many years, almost nothing has been done to apply it on a large scale. In the development of our industrial health services the emphasis has been on factory inspection—largely from a safety point of view—on the one hand, and health care by industrial medical officers on the other. In these aspects of occupational health, and also in factory legislation and notification of occupational disease, we have been pioneers and still have probably the finest services in existence. Unfortunately this is not true of our occupational hygiene facilities. Indeed no service of this kind exists and our country lags behind others.

AMERICAN PRACTICE

In the United States industrial health services developed rather differently. The great increase of production during the first world war resulted, as here, in outbreaks of industrial disease. To combat these, individual States set up divisions of industrial (or occupational) hygiene, usually as a branch of the State public-health department. These developed greatly between the two wars and now most States, and even some cities, have such divisions. They are based on a laboratory where physicians, engineers, chemists, and industrial nurses work together on occupational health problems. Each specialist lends his particular skill to the task. For example, a visiting factory inspector or nurse may be the first to discover a possible toxic hazard. The physician may then visit the factory and, by studying the environment, talking with management and workers, and making clinical and laboratory examinations of those likely to be affected, decide whether a health hazard exists. Chemists and engineers then survey the factory, taking air-samples in different parts, and measure the amount of toxic substance present in the air. If a health hazard is discovered the correct preventive action can be determined in the light of the known facts. In this the engineer, with his special knowledge of exhaust ventilation and other protective devices, plays a large part.

These laboratories carry a full range of equipment for assessing most physical hazards in industry. Thus they are able to analyse air and body-fluids for toxic substances, to perform dust-counts and analyses, measure radiation, and conduct lighting and thermal comfort surveys. An important point is that they are not organised for research, though research is of course done. Their main work is to help and advise industry in health. Much of the work is routine—for instance, repeated examinations in lead-works of air-samples, and urine and blood specimens. In this country there are no facilities for regular surveys of this kind, apart from blood-counts, except where the firms provide them. The occupational hygiene division also acts as an advisory centre on all matters of occupational health. Help is given to firms which wish to start their own medical services, and there is often an industrial nursing consultant who acts as focal point and adviser to all industrial nurses in the area.

Many other countries have developed such services—e.g., Canada, Finland, Peru, the Philippines, Sweden, the U.S.S.R., and Yugoslavia.

A FIRST STEP

I believe that there is a real need for a service of this kind. Anyone with access to a large number of factories, as we have at Slough, must come to realise that there is a great deal of occupational ill health which is never recognised, let alone notified. Through ignorance dangerous solvents and other toxic substances are used carelessly, and may cause disease which long remains undiagnosed. Men are also often exposed to high concentrations of the less dangerous solvents, and minor health impairments or worry over the effect of the fumes may lead to loss of production. Fettlers and grinders may work in confined spaces with high dust-concentration, their only protection a calico mask which they are expected to wear continuously. Often lighting, heating, or ventilation is poor, and recurrent though preventable eye injuries are found.

These situations arise because managements of small firms are not in a position to obtain advice on health matters. When advice is given in convincing form, they are usually anxious to coöperate and improve working conditions. A detailed survey of conditions, from medical and engineering aspects, figures for air-concentrations, and suggestions for action are far more effective in producing a positive response from management than mere verbal arguments.

The Factory Department of the Ministry of Labour and National Service has 16 medical inspectors of factories who are responsible for the whole of England, Scotland, and Wales. These inspectors have a wider knowledge of occupational hygiene than anyone else in the country, yet they have no technical assistants and no suitable laboratory behind them. Samples for analysis are sent to the Government Laboratory and, because only occasional samples can be analysed, few, if any, complete and repeated occupational hygiene surveys can be made. The situation would be very different could there be many more medical inspectors and regional laboratories, with engineers and chemists, to help them. The Medical Research Council's Unit for Research in Industrial Medicine has a fine laboratory and is able to undertake any kind of factory survey, clinical or environmental. It, however, exists primarily for research—and rightly so—and cannot carry out routine work or cope with the many small problems that exist up and down the country. Really serious hazards—such as instances of beryllium poisoning or the recent outbreaks of poisoning by dinitro-*ortho*-cresol—are dealt with immediately and effectively, yet the multitude of smaller problems cause greater loss of health and production.

Realising the need for this preventive approach to occupational health, the Nuffield Foundation and those working at Slough were responsible, in 1949, for sending an engineer, Mr. R. J. Sherwood, to Harvard to be trained in occupational hygiene techniques. After his return a small team was formed, consisting of myself as physician, Mr. Sherwood as engineer, and Miss Joan Bedford as chemist, to investigate occupational health problems at Slough and elsewhere. The foundation made a grant towards an occupational hygiene laboratory which has been set up at the London School of Hygiene and Tropical Medicine. Samples collected in the field are brought to this laboratory for analysis, counting, and so on. The laboratory is part of the occupational health sub-unit which also plays a part in teaching students of the D.P.H. (industrial elective) course and public-health engineers.

The number of requests for help which we have received has been greater than so small a unit can cope with. As well as the regular work at Slough on the discovery and control of toxic hazards, skin irritants, and uncomfortable working conditions, there have been requests for advice from managements who were about to instal new processes or who wished to check safeguards

which they had installed. We have also had many calls for advice from industrial medical officers or direct from managements of firms in all parts of the country. Our experience has convinced us of the need for a service which can give technical help to industrial medical officers and, even more, to firms with no medical care. An occupational hygiene service to cover the entire country would need perhaps six or eight units, staffed with doctors, engineers, chemists, and physicists. If any industrial health service was later set up these centres could form an integral part of it.

A NATIONAL SERVICE

A precedent for these centres already exists in the Public Health Laboratory Service, which is administered by the Medical Research Council. There are 18 special or reference laboratories and a further 49 constituent laboratories in different parts of the country. Nothing like this number of occupational hygiene centres would be needed, but their administration by the Medical Research Council for the Ministry of Health following the pattern of the P.H.L.S. is a possibility.

There is also a strong case for the centres to become part of the Factory Department of the Ministry of Labour and National Service. This department has the necessary experience and a corps of medical inspectors who could act as leaders of the project. Further, the work of the service would be largely inspection, using every available scientific means, rather than research.

Another possibility is that industry itself should be encouraged to set up these centres. The National Coal Board, for instance, is already doing, and planning to do, preventive work based on research carried out by the Pneumoconiosis Research Unit of the Medical Research Council. The Industrial Hygiene Research Laboratory of Imperial Chemical Industries is an example of what a single large firm can do. Other large firms might do the same, but in many the hazards are not numerous enough to warrant such provision. Some industrial organisations, such as the Shirley Institute (cotton), the British Cast Iron Reserach Association, and the British Iron and Steel Research Association, already carry out some occupational hygiene investigations, though they are not primarily interested in health. Some of them are associated with the Department of Scientific and Industrial Research, which suggests the possibility of a combined private enterprise and Governmental approach.

Finally, some universities might consider it of value, from the point of view of teaching, to join in work of this kind, perhaps in coöperation with another agency such as the Factory Department. But whatever the form of organisation chosen, it is important that something should be started now. The health of our workers and the output of our factories should no longer be allowed to suffer for want of reasonable facilities in occupational hygiene.

I should like to place on record the names of those who foresaw the need for occupational hygiene at Slough and elsewhere in this country, and were responsible for sending the first engineer to train under Prof. Philip Drinker at the Harvard School of Public Health. They are Dr. A. Austin Eagger, Prof. J. M. Mackintosh, and Dr. M. E. M. Herford.

Poliomyelitis

In the week ended Aug. 23 notifications (uncorrected) of poliomyelitis in England and Wales were as follows (figures for the previous week in parentheses): paralytic 152 (170); non-paralytic 68 (88); total 220 (258). This brings the total for the 34 weeks since the start of the year to 2388, compared with the following totals for the same period in each of the five previous years: 1951, 1747; 1950, 4125; 1949, 2033; 1948, 1067; 1947, 3619.

According to the Weekly Epidemiological Record, issued by the World Health Organisation, there has been a definite recrudescence of the disease in Europe, and notably in parts of Western Germany, the Netherlands, and Belgium. In the U.S.A.[1] 2648 cases were reported during the week ended Aug. 9; this was an increase of 15% over the figure for the previous week. Up to Aug. 9 the cumulative total for the "disease year," which began with the week ended April 5, was 12,046; the corresponding figure last year was 7056. The incidence has also been increasing in Canada, particularly in the west, where quarantine restrictions have been imposed at two large military stations, from one of which 17 cases had been reported.[2]

International Certificates of Vaccination

The International Sanitary Regulations adopted by the Fourth World Health Assembly come into force on Oct. 1. New and simpler forms of certificates of vaccination against smallpox and cholera will then be used.

Persons going abroad, who are vaccinated against these diseases *after* that date, should have their certificates on the new forms, obtainable from the company arranging their passage. International certificates for vaccination done *before* that date remain valid for the period shown on them.

The international certificate of vaccination against typhus has been abandoned, because this vaccination is no longer required internationally.

Medicine and the Law

Murder and Abnormality

THERE is notoriously an unbridged gulf between the forensic and the medical view of insanity in relation to criminal responsibility. Two recent cases in the Court of Criminal Appeal show afresh how far the two are apart.

On the appeal of J. H. Godar,[1] convicted of murdering Maureen Cox, his counsel, Mr. G. D. Roberts, Q.C., conceded that at the trial the summing up had been full and fair and that there had been evidence on which the jury could properly find a verdict of guilty; in other words there were no grounds for an appeal. It appeared that Godar had in 1944, while serving in the Army, been found to be suffering from a disease of the mind amounting to defect of reason. This fact, however, was not mentioned as a matter for the appellate tribunal to consider; it was merely referred to by counsel, in passing, as one which the Home Secretary might perhaps take into account when advising the Crown as to the exercise of the prerogative of mercy.

On the other appeal, that of J. T. Straffen,[2] the apparent irrelevance of the appellant's mentality was even more striking. At his trial there had been evidence of his having been certified a mental defective, of his having formerly been found unfit to plead to a criminal charge, and of his having strangled two other little girls in addition to the 5-year-old Linda Bowyer whom he was accused of having murdered.[3] The Court of Criminal Appeal was not asked to note his obvious abnormality; it was irrelevant; the two grounds of appeal (technical questions of the admissibility of evidence, legally, no doubt, of great importance) ignored it. Even had the case found its way up to the House of Lords, his mental condition would still doubtless have been immaterial. Public opinion, as well as medical science, may be convinced of the irresponsibility of men like Straffen. The criminal law goes on its majestic way unconcerned.

"There are," wrote the late Sir Edward Troup, a former head of the Home Office, "a certain number of borderline cases in which the question whether a prisoner is insane,

1. Morbidity and Mortality: Weekly report by the Federal Security Agency, Public Health Service. Washington, D.C., Aug. 15, 1952.
2. *Times*, Aug. 29.
3. *Ibid.*, Aug. 20.
4. *Ibid.*, Aug. 21.
5. *Lancet*, Aug. 2, 1952, p. 239.

though negatived by the jury or not raised at the trial, has to be considered after conviction." If medical experts then certify the prisoner insane, "there is a consensus of legal authority for the view that it would be contrary to the common law to allow the execution, and the records which go back to 1840 show no exception to this rule." Accordingly on the advice of his panel of doctors the Home Secretary has recommended that Straffen should be reprieved. Thus, in the end, the medical opinion prevails over the judicial sentence after all. Sir Edward went on to give statistics showing that, over the 22 years from 1901 to 1922, out of 585 persons convicted of murder 517 were found to be insane, either before trial or by special verdict of the jury or on Home Office inquiry after conviction. If, as is probable, more recent totals show a not dissimilar proportion, is it not time for another review of insanity in relation to crime such as that which the Atkin Committee conducted thirty years ago? As Sir Russell Brain, P.R.C.P., has pointed out[6] the circumstances in which mental illness should mitigate criminal responsibility "is a question, not for lawyers or doctors, but for society to decide"; and he, too, thinks the question should be reconsidered, perhaps by a Royal Commission.

Points of View

CURE OF TOBACCO-SMOKING

LENNOX JOHNSTON
M.B. Glasg.

"How can I stop smoking?" I, who stopped many years ago, have often been asked. "By not smoking again," is the brutal correct answer; for every movement of smoking is voluntary. "But I have tried repeatedly and failed; I haven't enough will-power. Is there a way in which I can be helped to stop?" "Yes, there is a way," is the answer; and the purpose of this article is to show it.

The view that smoking can be stopped only by the exercise of will-power is almost universally accepted. Yet it is only part of the truth. For "knowledge is power" (or will-power) when acted upon. The greater the volume and more impressive the character of knowledge, the more insistently does it demand effective expression (in action). When knowledge is repressed, or is merely expressed in words unsupported by actions (when, for example, a smoker says, "I *know* that smoking is harmful" but continues to smoke), the power of knowledge is insufficient (usually because of insufficiency of knowledge) to compel its effective expression.

The urge to smoke is at first purely psychological—a desire. While it remains so, it is easy to give up smoking. As smoking proceeds, however, the urge becomes increasingly compulsive: the psychological urge has been reinforced by a pharmacological urge, the craving for tobacco.

PSYCHOLOGICAL URGES TO SMOKE

The desire to smoke originates from the advocacy of smoking by smokers, much of it unconscious. Each time a smoker lights up, he says in effect, "I am in favour of the smoking of tobacco, I approve of smoking", and little weight attaches to any mere words he may utter in contradiction to his actions. Each proferred cigarette, each word of approval of smoking, written or verbal, is smoking propaganda. Every smoker is, in fact, whether he wills it or not, a living advertisement for tobacco, and there are so many smokers today, and they smoke and speak encouragement to smoke so often, that the persuasive pressure on non-smokers to commence or recommence smoking is powerful indeed. To this must be added the lavish scientific advertising of the tobacco combines. In the United States of America in 1945 it was calculated that almost 3000 non-smokers start to smoke every day.[1]

The initial desire to smoke is closely associated as a rule with one to appear grown-up or sophisticated, to imitate someone admired—usually Daddy or, nowadays, Mummy—or to be companionable or sociable. Later there is a recurring desire to perform the now largely habitual and often ritualistic actions of smoking, particularly at certain times—e.g., after meals—or to relieve boredom or nervousness. Freud drew attention to the possibility that oral-libidinal satisfaction—the association of smoking with the infantile pleasure of suckling—may also urge people to smoke.[2]

Psychological "infection" of the non-smoker is completed, as a rule, by the intimate persuasion of a smoker: "have a cigarette, old man"; "it'll do you good (or steady your nerves)"; "don't be so miserable (or a cissy)"; "one has to have a bit of pleasure (or comfort) these days"; or "one has to have one little vice; it doesn't do to be too good." Besides simple persuasion, reinforced by example and free samples, smokers use—though as a rule without realising it—less ethical methods of infecting non-smokers. Thus they suppress the facts, particularly the more damning facts, against smoking, and circulate in their place favourable untruths: in short, they use deception.

PHARMACOLOGICAL URGES TO SMOKE

Having established, on myself and 35 volunteers, that the repeated administration of nicotine is a satisfactory substitute for tobacco-smoking,[3] I decided to ascertain how long craving for a drug of addiction takes to develop.

I was at that time somewhat addicted to nicotine, so I had to use another drug. I gave myself hypodermically, night and morning, cocaine hydrochloride, a drug I had not taken previously, in doses ranging from $^1/_4$ to 1 grain (16–64 mg.). About 5 min. after administering each dose, I experienced a curious sensation which I find impossible to describe: it was readily distinguishable from nicotine and codeine (whose actions are equally indescribable), but was not pleasurable. This occasioned me and a control volunteer to whom I administered several doses, some surprise—and, indeed, disappointment, for we had recently had considerable pleasure from experimental doses of nicotine. About 10 days after commencing the administration of cocaine, I found myself looking forward to the next dose with considerable satisfaction, and after 25 doses deemed it advisable to discontinue the experiment lest I became strongly addicted.

The slight craving I had acquired lasted several days, and could readily be recalled in fantasy for a much longer period. It must have developed as a side action of cocaine, and been built up cumulatively. With the craving came pleasure on its appeasement; and it seems clear that the pleasure derived from drugs of addiction arises mainly from the appeasement of craving, once such craving has been acquired. Pharmacological craving is clearly a specific, abnormal appetite for a drug, hostile (because of the drug's toxicity) to the normal, though not to the abnormal, functioning of the organism. Its development completes a vicious circle: administration gives rise, though not immediately, to craving, which leads to further administration. Once set in motion, this circle continues to turn without, as a rule, interference from the smoker's will.

Besides appeasing the craving of addicts, drugs of addiction have a further immediate specific pharma-

6. *Times*, Sept. 1.

1. Clean Air. No. 39. April–June, 1948, p. 4.
2. Freud, S. Three Essays on the Theory of Sexuality. Translated by James Strachey. 1949; p. 61.
3. Johnston, L. *Lancet*, 1942, ii, 742.

cological action on both addicts and non-addicts. Smokers do not enjoy the pharmacological action of tobacco smoke at first—indeed, they usually dislike it. But as time goes on they find that, besides deriving positive pleasure from the appeasement of their craving, they have, if they be inhalers, an almost instantaneous general analgesic against life's little, or even big, stresses and vexations. The inhalation of cigarette smoke in moments of severe stress, in fact, is reminiscent of the inhalation of gas-and-air by a woman in labour. In pipe-smoking, the analgesic (or sedative) effect is delayed for about 10 minutes, since the absorption of nicotine is mainly alimentary. Unfortunately, the pleasurable analgesic action of nicotine (and of other drugs of addiction) is more than offset by after-depression and apathy. This cannot, of course, be demonstrated, since changes in mood are subjective; but I have observed that a striking and sustained uplift of spirits and of general interest almost invariably accompanies the giving up of smoking; and that heavy smokers seem as a class more depressed ("fed up") than non-smokers.

The effects of the psychological and pharmacological urges cannot be separately demonstrated, nor can their relative strengths be measured; only their combined effect on conduct is obvious. But interrogation of (I estimate) about 10,000 cured smokers over the past 24 years, and a personal analysis based on stopping smoking four times (twice experimentally), and on taking some 200 doses of nicotine by various routes, have convinced me that the pharmacological craving for tobacco though strongly compulsive, at first, is short-lived, at any rate in its acute form. It reaches its peak 24–36 hours after smoking has been stopped and thereafter sharply and steadily declines, though the initial steepness of the decline is not maintained: it takes several months, indeed, to reach zero.

Psychological urges to smoke, on the other hand, do not decline steadily when smoking is stopped, since most of the psychological stimuli which produce them persist. In my case, the desire for the general analgesic action of nicotine persisted, in times of particular stress, for more than a decade; so also did the less compulsive urge to smoke for companionable reasons. The desire for a plaything—the wish to perform the habitual actions of smoking—scarcely troubled me, and could in any case have been almost completely satisfied by performing the actions of smoking without actually lighting the cigarette. The longing of the recently cured smoker, after a meal, is not to perform the habitual actions of smoking, but to administer his postprandial dose of nicotine.

If, after he has smoked for some time, the smoker loses desire to smoke, and wishes to stop smoking, a conflict develops between opposing urges—the will to stop smoking, on the one hand, and craving for tobacco reinforced by various psychological urges, on the other. If the smoker's will prevails, smoking is cured temporarily or permanently. If, however, his involuntary urges prevail, he continues to smoke; but his smoking no longer expresses his will. He therefore tends to repress the whole conflict, for the outcome has been damaging to his self-esteem. He attributes his smoking solely to socially approved urges such as habit, the relief of boredom, or a simple desire for enjoyment. Smokers who have tried unsuccessfully to stop smoking, though they seldom realise or admit it, are unwilling smokers.

All smokers, willing and unwilling, however, encourage the spread of smoking and add to tobacco consumption. This has risen in Great Britain from 166 million lb. in 1913, costing £8,300,000, to 281 million lb. in 1948, costing £42,800,000. The increase in smoking has resulted in the progressive elimination of one non-smokers' sanctuary after another—drawing-room, bedroom, workroom, place of entertainment, conveyance, and finally, of late years, hospital ward and sanatorium, even when and where patients seriously ill from respiratory diseases are under treatment. The problem of sanctuary for those who claim (as I do) that the right to breathe clean air—air free, at any rate, from irritant fumes—is as basic, in a civilised country, as the right to drink clean water, has become today almost insoluble even when they are ill.

HOW TO STOP SMOKING

It is difficult to stop smoking—very difficult indeed if one is a heavy smoker of long duration. In order to stop, it is necessary to do much more than merely decide. Intellectual conviction that smoking should be abandoned is an essential preliminary, of course, to stopping, but it is only a preliminary. There must also be a build-up of resolution sufficient to withstand indefinitely all urges to smoke. As in war, the more overwhelming the preparatory build-up of strength (or resolution), the easier and more certain the victory; and conversely, irresolution tends to prolong the struggle and jeopardise success. Resolution not to smoke is born, as already indicated, of a sound and clear, though not necessarily extensive, knowledge of the action of tobacco smoke on the human organism.

The most difficult task, as a rule, is to make the break—to withstand the first surge of craving. Half the battle is over when the first day and night of non-smoking are completed. It is best, in my experience, to stop suddenly, abruptly, completely, ignoring all symptoms which might possibly be associated with tobacco deprivation. Detoxication, and hence improvement in health, begin directly smoking is discontinued, no matter how the smoker may feel; so he must follow his purpose without regard to his feelings. All thoughts about smoking should be rigorously excluded from consciousness, because craving precludes, for a time, objective thinking on this subject. It may help if he treats the craving contemptuously from the start, by carrying for a time (while resolution runs high) the paraphernalia of smoking. The more inflexible the determination to end smoking, the less the pain: as in grasping nettles, pain varies inversely with firmness. It is well to proceed silently, unobtrusively: the raillery of smokers is shrewdly calculated to undermine resolution. Acute affections, particularly respiratory affections, temporarily remove or greatly reduce all urges to smoke. A good time to stop, therefore, is when such an affection develops; or respiratory inflammation may be produced artificially, to some extent, by smoking very heavily the night before.

Psychotherapy consists in building up the patient's determination to end smoking by persuasion, encouragement, undeception, and re-education—patient and oft repeated when necessary—until, in favourable cases, its expression in non-smoking becomes irresistible. Fear, particularly of lung cancer (though this is a long-term risk) can be a potent psychotherapeutic agent, and the use of such intimidation is clearly justified when—as in this case—it is based on fact, or at any rate strong probability. A first, often difficult, task is to dispel defeatism born of previous, sometimes repeated, failure—failure almost invariably associated with ignorance of essential facts about smoking. Friends ought perhaps to be warned against irritability; but I believe I displayed none, and I suspect that it may in some cases be "laid on" by the smoker in the hope of getting his wife or fiancée to entreat him to recommence smoking, and thus shoulder some of the blame for relapse.

Unless psychotherapy has been extremely thorough, there is great risk, with so much psychological infection about, of relapse, particularly at times of lowered resistance—e.g., on sociable occasions, or in moments of stress. To avoid this,

it is best to go over to the offensive: the oftener and the more remorselessly one attacks the smoking of others and exposes the falsity of arguments in favour of smoking (while doing one's best to avoid giving offence), the more finally is one committed to non-smoking, and the less one's danger of relapse. As cure is consolidated, and understanding of the harm caused by tobacco-smoking deepens, there develops gradually and unconsciously a hardening of one's attitude, or even hatred of tobacco-smoking, with pity for tobacco-smokers.

THE TOBACCO TABOO

Smokers dislike contemplating the ill effects of smoking, for some of which they cannot escape responsibility—the ash, the ends, the fumes, the fires, and the damage to the health, happiness, and economy of individuals and nations. They tend to repress them, and hence dislike hearing them spoken of. Thus they discourage serious discussion of the subject, imposing, in fact, a "drug taboo." Those who, in defiance of the taboo, speak out about the ill effects of smoking, are disapproved, derided, or ostracised in proportion to their outspokenness. Public lectures, including radio talks, which give *without compromise* the medical facts about tobacco-smoking are unheard of. The more winged the phrase, the more pointed the argument against smoking, the less the chance of their publication in the press. Even the medical press shows reluctance to publish uncompromisingly anti-smoking matter. The most remarkable manifestation of the tobacco taboo is the omission from all standard textbooks on medicine of any account of nicotinism.

SMOKERS' UNTRUTHS

Smokers' untruths are not as a rule intentional—they are rationalisations rather than lies, and are the more deceptive on that account. Moreover, liberties taken with the drug taboo, like those taken with sex and religious taboos, are a fruitful source of humour. Jokes about alcohol are, of course, legion, but there are also many about tobacco: references to cigarettes as "gaspers" or "coffin-nails" are examples. Most of us, hearing little about smoking except this language of untruths and jokes, grow up ignorant or deceived about the facts, and are psychologically infected by nicotinism in our 'teens or before.

After smoking has started, the development of craving for tobacco is evidenced not only in increasing application to the drug, but in increasing resistance to undeception. As a result, confirmed smokers are often largely inaccessible to the facts against smoking: the simple deception which took in the "pre-smoker" becomes, with development of craving, an increasingly fixed delusion of the smoker. But the inaccessibility varies. Some smokers are almost wholly inaccessible, refusing to concede the validity of even the most obvious fact against smoking; others listen with full attention, and concede verbally even the most hostile facts. Unless, however, words are supported by deeds, the sincerity of such agreement must always be in doubt. The fixity of smokers' delusions is doubtless related to the strength of their craving for tobacco, and in many cases this is so strong that the smoker projects his repressed self-criticism on to his would-be undeceiver, characterising him as a crank or fanatic, or at the least, as hopelessly biased.

Smokers usually refer to tobacco as something good or desirable which adds to the joy of living—not quite a necessity, but at any rate a luxury. Officially it is treated, in fact, almost as a necessity: even when our shipping position was at its worst during the war, space was found to bring us huge quantities. Yet tobacco is not a luxury; even on addicts, the whole action is not luxurious: coming out of their drug, smokers are depressed, like addicts of other drugs. If tobacco is a luxury, opium is an even greater luxury, and has an even stronger claim to be treated as such. Actually tobacco smoke contains various poisons, notably nicotine, pyridine bases, carbon monoxide, and arsenic,[4] and it is clearly asocial to pretend this toxic drug is a beneficent luxury. Addiction to tobacco, like addiction to opium, is a specific disease—an intermittent intoxication. An almost universal delusion is that smoking is a vice—a moral, not a medical, issue. Vice (or moral degeneracy) is merely a symptom common to all drug addictions. It is revealed in the common disregard of smokers of the moral rights of non-smokers. I have been in homes where the feeding and clothing of the children were deplorable, yet the parent or parents spent relatively large sums (perhaps £1 a week out of a weekly income of £7) on tobacco.

A common minor delusion of smokers is that they get their pleasure from purely psychological factors—playing with the cigarette or lighter, sucking the pipe or watching the smoke. Smoking, they say, is not enjoyed in the dark, or by the blind. In fact, of course, smoking in darkened cinemas is widespread, and the blind are just as strongly addicted to tobacco as the sighted. An undeniable advantage of smoking is its sociability; but actions which are sociable are not necessarily social. "Thick as thieves," we say, meaning, I take it, that thieving is often sociable; but it is also asocial, like drug taking.

The symptoms of tobacco-smoking become apparent to the sufferer only after the disease has been arrested, and he has given up smoking. An accession of high spirits, energy, appetite, and sexual potency, with recession of coughing, makes the chief symptoms of tobacco-smoking plain. Moreover, an increase in weight, often measurable in stones rather than pounds, in the course of a few months, shows that tobacco-smoking usually interferes with nutrition—a fact which should be sufficient in itself to cause smoking to be forbidden in sanatoria.

Tobacco-smoking is not, of course, usually a seriously incapacitating or a directly killing disease; but that does not mean its effects on health are negligible. Its protracted course, the enormous numbers affected, and spreading infection make smoking one of our most serious diseases. The extensive published work on tobacco-smoking as a predisposing cause of other disorders has recently been reviewed by Scott.[5] Wynder and Graham,[6] and Levin, Goldstein, and Gerhardt,[7] in America, and Doll and Bradford Hill [8] in this country, have established a strong probability that the development of carcinoma of lung is favoured by tobacco-smoking, and this probability was strengthened by the observations of Dungal.[9] Deaths from carcinoma of lung have risen from 612 in 1922 to 11,272 in 1949—a rise of 1740% in twenty-seven years, or 64% per annum. The work of Pearl [10] shows the total effects of smoking on mortality. Smokers of ten or more cigarettes a day aged 30–45 have a mortality from all causes considerably more than double that of non-smokers. This heavy toll of human life at a comparatively early age has not been sufficiently recognised.

These facts have failed to stir our profession to action. The reason is not far to seek: about 80% of us, I estimate, are smokers, and we behave collectively like an addict of tobacco. Radical cure of tobacco-smoking lies in its prevention; and tobacco-smoking is no more difficult to prevent than opium smoking. Our duty is plain.

4. Dixon, W. E. *Brit. med. J.* 1927, ii, 719.
5. Scott, R. B. *Ibid*, 1952, i, 671.
6. Wynder, E. L., Graham, E. A. *J. Amer. med. Ass.* 1950, **143**, 329.
7. Levin, M. L., Goldstein, H., Gerhardt, P. R. *Ibid*, p. 336.
8. Doll, R., Hill, A. B. *Brit. med. Jour.* 1950, ii, 739.
9. Dungal, N. *Lancet*, 1950, ii, 245.
10. Pearl, R. *Science*, 1938, ii, 216.

In England Now

A Running Commentary by Peripatetic Correspondents

"THEY order this matter better in France." What it was that was better ordered Sterne does not tell us, but I think I have found an answer.

Large numbers of the French embellish my practice. I really mean embellish, for consultations with that race are strenuous, exciting, even explosive, but never dull. I count among my most valued patients an ancient wrinkled peasant woman, equipped with all the shrewdness and capacity for clear thought which springs so naturally from the soil of France.

She complained that things did not march as they should over the last few years. A lack of energy, not much, mais quand même. A certain slowing of the tempo of life of the most mysterious. What could it be, one asked oneself?

At the end of the consultation I found myself somewhat embarrassed, and glad that I had to talk in French. I am less easily understood in that language, and I did not want to be understood too easily. A puzzled expression rested on her brow as I haltingly fished from the corners of my memory words sufficiently vague to suggest without saying outright that after four score years it is the nature of things to feel a little less energetic than in the past: that at times we might even, without alarm bien entendu, experience a passing weakness.

Weakness! That did it. By sheer luck I had the right word, a word which could partner the ailments of the young as well as of the old. Her face lit up, as only the face of a Frenchwoman can when an explanation strikes home and her mind is set at rest. "Oui," she said with great satisfaction, "C'est ça. C'est la grande faiblesse. Voilà!"

I felt in my own mind an answering echo to her satisfaction. Who would mind suffering from la grande faiblesse? I feel I could even die of it in the grand manner, calmly and with dignity. But to succumb wretchedly to its English counterpart—what would it be, senile debility?—perish the thought.

That is at least one of the things they order better in France. They ennoble the commonplace with a gracious dignity of expression mixed with a sense of the dramatic. I wish I had had to write a certificate for the old lady. No printed slip for her! A grand flourish with a goose-quill on the finest parchment—that alone would have been fitting.

* * *

The children—not mine unfortunately—found a fledgling thrush fallen from the nest. They fed it on worms which it engulfed greedily; but, as so often happens, the ungrateful bird died untimely, mysteriously and undiagnosed. The case did not come to autopsy, but a conference was held to consider in what respects therapy had been inadequate. "I know what we ought to have done," said Bridget. "We ought to have chewed the worms first." Next time she will, for she's a kind girl to birds, though perhaps less so to worms.

* * *

Having recently had occasion to inquire into the possibility of purchasing some electrical apparatus, we found ourselves led insensibly into a series of communications with an old-established French firm. Our latest receipt in this correspondence is a schedule entitled *Conditions de vente*, which appears to contain the nub or crux of the projected transaction. It is a complicated document, and after several pages concerned with such matters as *expedition*, *délai*, &c., we came at last to the vital factor of *prix*. This factor proved unexpectedly difficult to elucidate, being surrounded by a scientific smoke-screen of Gallic exuberance and plasticity. The section began forbiddingly:

"*Nos prix sont révisables suivant la formule*

$$P = P_o \left(0{,}10 + 0{,}80 \frac{S}{S_o} + 0{,}10 \frac{M}{M_o} \right)$$

où les différents paramètres sont définis ainsi :— . . ."

But we are made of stern stuff, undaunted by income-tax schedules and claims for mileage allowance; dragging to our bosom our invaluable New Little Larousse, we ploughed on. It appeared that P was the definitive price, P_o the estimated price, S the index of wages in the Electrical and related industries published (and rectified globally) by a mysterious body designated R.G.E. two months before the actual date of delivery, and S_o the index for the fortnight preceding the date of the estimate. M_o was the price of aluminium in sheets of 1 mm. (R.G.E.), and M the value on the last day of the first two-thirds of the actual delay in delivery. When we had got thus far our attention was distracted by a musical plash, and we observed with interest that a drop of sweat from our overheated brow had fallen on the paper. All we had wanted originally was a galvanometer, but we no longer felt the desire.

On the other hand, when we showed the document to one of our clinical colleagues who is still fortunate enough to have a few private patients he was at once interested, and he has produced a sliding scale of fees based on a similar principle. His final charge (F) is related to the estimate given to the patient (E) by the following equation:

$$F = E \left(0{\cdot}1 + 0{\cdot}5 \frac{C}{C_o} + 0{\cdot}2 \frac{P}{P_o} + 0{\cdot}2 \frac{T}{T_o} \right)^n + \sqrt{D_c . D_w}$$

where C is the mean cost-of-living index in the period between the operation and the rendering of the account, and C_o the index figure at the time of arranging admission. P and P_o represent the corresponding figures for the cost of petrol, and T and T_o those for telephone rental. D_c and D_w represent physical depreciation of our colleague and his wife in units of earning and coping capacity respectively, and the exponential n has been added by a statistical friend who feels vaguely uneasy without it.

* * *

Readers of the *Britannica Book of the Year* for 1951[1] must prepare for a serious shock when they turn to the section headed "Words and Meanings, New." If they can support "depurged" for "one restored to acceptable political or other standing," and are able to picture their charlady as an "accommodater"—surely the gracious old word "obliger" should be retained?—they will still have to face a shocking debasement of the term "bogey." This noble description of a golfer's performance stands, in this country, for the perfect score for a hole; and a "birdie," of course, describes a hole done in one less than bogey, while an "eagle" is reserved for the rare feat of doing a hole in two under bogey. Now, it seems, our golfing colleagues in the United States have begun to apply the noun "bogey" to a hole done in one over par (par being the perfect score for the hole), while double-bogey is used for two strokes more than par; and what is worse, they also use these terms as verbs. At this corruption of long-accepted usage we can only shake grave heads.

* * *

On stopping in our local mountain hut the other week-end for sodden sandwiches and cold tea, we found the following entry neatly written in purple ink in the visitors' book:

"I hitch-hike from my home in Spa to Ostend, then in the steamer I came to Dover, then again I hitch-hike to Birmingham, Glasgow, Aberdeen, and Balmoral, where it was raining much. There as I standed in the downpour I saw your lovely Queen, who smiled and waved to me, yes to me, a poor little wet tramp, as she drive to the church, and I could see her say 'Good morning.' I am quite comeover. Now I am in this hut for two nights and I have no food and still it is raining very much, and I am off to Aviemore. God bless those who maintain this hut; God bless your beautiful Queen; God bless the whole British people."

The hut is situated in one of the remoter fastnesses of the Cairngorms, and is reached by a mountain pass strewn with large boulders, liberally interspersed with bog and torrent. In these days of restriction, gloom, pessimism, and complaint, we feel that our Belgian visitor's exuberant good will in the face of considerable adversity should be something of an object lesson.

* * *

The Safe Food Campaign.—Notice in a café in Essex: "All crockery used in this establishment is sterilised each week."

1. London: Encyclopædia Britannica Ltd. 1952. Pp. 692. £3 3s.

Letters to the Editor

THE PROSPECT OF GENERAL PRACTICE

SIR,—As a young general practitioner I find myself in complete disagreement with the conclusions of your correspondent (Aug. 16). At medical school my teachers did not deride general practitioners but named certain good ones and demonstrated their letters as examples of clinical judgment and observation. Some of those whom I knew personally excited my admiration and respect as much as my hospital chiefs did, so I entered general practice biased for, rather than against, it. After 5 years in it I would not change my job, and to find out why, I asked myself the questions which your correspondent answered with such crushing negatives.

1. Have I got conditions of work which allow me to exercise my technical skill and satisfy my intellectual thirst? Yes. In a moderate-sized partnership I do have time to examine my patients. I have no less equipment in my consulting-room than the specialist has in his; but, although I do not personally carry out barium meals, blood and chemical examinations, electrocardiographs, and so on, my interest in the result of these tests is no less and my satisfaction is as great if they prove me right. And my opportunities for follow-up are considerably greater: my patients give me no option but to follow them up, whereas the specialist often depends on me for further news of them.

2. Can I provide a happy family life for my children and bring them up in conditions which will let them be moderately civilised and well educated? Yes. Although I have to work harder than most men for a decent living, I do not need to put in the hours your correspondent suggests. My wife must answer telephones and doorbells on top of her domestic duties; but since she, I, or some other responsible person must always be in the house anyway for the children this is not quite the tie it seems. When one of my partners is on duty we can go out together, and local help is as willing to come to a doctor's house as to any other. Our children, it is true, must not scream and shout immediately outside the consulting-room door; but this is no great hardship for them. And since I did not find among my school and university contemporaries that doctors' sons were less civilised than other people's I do not worry on that score.

3. Does general practice allow me to work without thought of gain? No, but what occupation does? The well-educated member of any profession would surely spend more time in the theatre and the art gallery and less at his work if he were free from that stimulus. What could be more civilised for the salaried G.P. than to drop 1000 patients and devote the time gained to reading philosophy or playing the flute? Am I blackmailed by hostile circumstances? No. Legally the patient has the whip hand; but if he is thoughtless or stupid, or makes unnecessary demands, I no more hesitate to tell him so than my father did his private patients a generation ago. I lose no more patients in this way than I gain through my rivals taking the same line. The patient may report me to the executive council, but unless he has a genuine grievance he involves me in no more than an explanatory letter.

4. If my health falters my livelihood is endangered, but no more so than in any other job. The edicts of the Ministry of Health can surely seldom conflict with anybody's principles, and its regional medical officers do not spend their time searching our records for mistakes. As for the threat of my competitor getting a seat on the regional board, this would delight me because his administrative duties would leave him less time to compete against me without in any way increasing his attraction to my patients.

I do not wish to idealise general practice. It is hard work—it has its frustrations and annoyances, and it involves too much routine paper work—but it can be spiritually and intellectually satisfying and I believe in its future. It is important that good doctors should continue to be attracted to it; and for this reason articles like your correspondent's, which give a false picture, should be answered.

Newcastle upon Tyne. ANDREW SMITH.

SIR,—I would like to support Dr. Hanratty (Aug. 23) in his reply to your anonymous correspondent. General practice has always been just what the individual practitioner wished to make of it. This, for many of us, is its charm. In many ways this is more true now than ever before. Freed from the bar of money, a doctor can follow his cases as far as he wishes.

As for the "insults, stupidity, thoughtlessness, and unnecessary demands" of his patients, it is obvious that your correspondent has never thought of himself as the family doctor who is not only an adviser but a friend. Patients do not treat their doctors thus unless goaded by the unfriendly and unwilling attitude of the doctor. In my practice unnecessary calls are extremely rare; and night calls, apart from midwifery, very rare indeed.

There will be no research in general practice as long as the conception of research is one of a technical process requiring expensive apparatus. To my mind the general practitioner's research should be careful observation of the vast quantities of clinical and social material at his disposal. He should be able to call upon the services of a department of social medicine to help him to collect and analyse the material.

Possibly your correspondent will be surprised to hear that I not only chose general practice, but I enjoy it and would choose it again. Perhaps there are dissatisfied practitioners. If there are, I suggest they cease to look for outside causes of their dissatisfaction and apply the remedy from within themselves.

York. F. CHARLOTTE NAISH.

SIR,—Your correspondent certainly "went to town." The prospect is not so melodramatic, though full of poetic justice.

We have produced a breed of academic medicos, "lily-livered" when it comes to facing clinical medicine in the great unknown—outside the hospital ward, outpatient department, or examination halls. If you want general practice you must go and get it by proving your individual intrinsic value to the individual patient. The patient that seeks a doctor out is worth twenty dished up to him by official assignment or in a clinic: the relationship, a very personal and intimate one, starts propitiously in this personal approach.

There are still many openings for the man of courage and initiative combined with ability and a vocational calling. Let him put up his plate in a large residential or populous district, or where studied report bemoans the lack of a good doctor—a complaint I hear often. He will not have to wait very long before he is established if he gives good service.

The dissatisfied patient—and there are many more of them now than when I started in practice—is waiting for a G.P. whom he can approach on an equal footing, prepared to give time and interest to his case. He does not want, and certainly will not regard, as his G.P. the pen-pushing Civil Service drudge to whom he goes for certificates which could be as easily obtained at the post office counter, and with less waiting.

When I see a few well-qualified young men—and women—with courage and a vocational urge to treat and heal the sick putting up their plates and ready to deliver the goods I shall feel happier about the future, not only of medicine, but of the young Elizabethans.

London, W.1. W. PINNINGTON JENSON.

SIR,—Your correspondent paints a grim picture; but it is the work of a blindfold artist, for he confesses that he has not done any general practice.

Your correspondent's remarks were answered specifically by Dr. Hanratty. I would only add, first, that general practice offers great scope for research,[1] particularly into old age and its problems; and, secondly,

1. See Fry, J. *Brit. med. J.* Aug 2, 1952, p. 249.

that hospitals are, in my experience, only too pleased to allow the G.P. to have direct access to laboratory and X-ray departments. If this cuts down their out-patients and prevents unnecessary admissions, so much the better.

Let us have criticism of general practice, but let it be first-hand. Sir, are you prepared to print an anonymous article by a G.P. on the Prospect of Academic Research?

London, W.11. L. MELVIN GREEN.

SIR,—It was with amazement that I read your correspondent's article. Not one word or thought of medicine as a vocation relieves this cry of woe. Surely he considered the attractions of other methods of earning a livelihood before he became disillusioned and entered his medical school to train as a doctor. Did he not realise that patients are ill during the night as well as during the day, and that office hours cannot be followed in medicine; or why else does he complain about the need to be available throughout the 24 hours?

A patient is a sick person—the same as any other of the writer's fellow men a day or a week ago, but now in pain or distress—not a creature apart, full of insults, stupidity, or wicked demands veiling his threat of legal action behind a whining plea for this and that. Now, as in the past, he is grateful for the care and attention given to him by his own doctor, and he is still the same person, "the victim of the often appalling mistakes," who appears tucked up in his hospital bed, and not a creature metamorphosed by the high technical skill of the consultant at the teaching hospital.

Let the writer analyse his training afresh. Does he wish to estimate each chemical abnormality, to have a radiograph for each râle and rhonchus, to record each extrasystole on shining paper—meanwhile what of the patients who lie in their homes while the scientifically trained doctor is cogitating over his tubes, his cardiographs, and radiographs. The patient will turn to the doctor who has learnt the art and science of diagnosis by observation and inspection, by bedside examination, and one who then can use his scientific background to call for tests from those working in laboratories.

The general practitioner has bowed to the seizure of his goodwill by the State, though he knows new and complicated problems have risen thereby—but he is still not salaried. We think that a salaried service will produce uniformity and loss of drive and ambition—abstract qualities that are difficult to formulate.

There are many outside general practice and on the threshold of medicine who do not know the anxieties and fears when one has the responsibility of a patient's life in one's hands—and the satisfied pleasure when that responsibility is discharged with credit. There are many who can only think of the team around the bed in the great teaching hospital, where the personal onus of care is not so heavily on one man, where the relatives are not watching each move and action, and where the patient's friends do not have to be met and spoken to each day.

No! General practice will still take many of the "good" doctors, and more will enter the ranks if others on the threshold stop crying when they see a little of the hardship and none of the rewards of this great vocation.

G.P.

SIR,—I read with mixed feelings of horror and indignation your correspondent's article. It is a complete travesty of the facts.

I have time, and am able, to investigate fully all patients needing it—X rays, full laboratory facilities, and hospital beds are at my disposal should I need them. I find, however, that I can do almost all medical investigation without hospital beds, reserving these for biopsies only; when a patient requires specialist treatment he usually attends the consultant with the investigations already completed.

If the practitioner is sympathetic and does a good job, prescribes for his patients what is good for them—not what they want—gives certificates where it is justifiable and refuses them otherwise (however much longer that may take) he will be respected by his patients; he will not be abused either literally or with thoughtlessness, and he will find peace and satisfaction in his work.

Surbiton, Surrey. DUNCAN MILNE.

SIR,—As a literary exercise The Prospect of General Practice would no doubt acquire high marks—but not from a general practitioner of any experience. Your correspondent has, it appears, spent his days so far in lofty academic circles. All he needs now is to spend a year or two in general practice which will be worth any amount of theorising on the subject. Research in general practice, one may remind him, will not come by sitting down and taking thought. It will have to come by patient waiting, and, as he correctly surmises, the duties of each day are sufficient in themselves.

General practice is only one division of medical practice, and those who follow it must be content to be G.P.s and nothing else. It is true that mistakes are made in general practice—some quite unforgivable—but one has only to read the daily papers to know of horrifying mistakes made in hospitals.

Your correspondent's gloomy views about bringing up his children, and about life in general practice, have no basis in fact. As one who has seen many years of it, I can safely say that general practice today is far more bearable than it was under the National Health Insurance. Patients are more considerate and are more prone to regard the doctor as a human being and not as an automaton. All the same it can be very exacting, and at times, even exhausting.

In conclusion I should like to assure your correspondent that, even though he and his like decide not to enter general practice, that particular division of medical labour will continue to carry out, satisfactorily in the main, the bulk of the medical work of the country as it always has done; and, taking it all in all, that work will compare favourably with anything that may be done in hospitals.

Brighton. G. L. DAVIES.

SIR,—As a final-year student, I find it alarming to have my intended branch of the profession denigrated by such remarks as "low professional standard and lack of opportunity for good work."

I have been privileged to accompany a G.P. on his rounds and attend his surgeries, and I was impressed by the modern techniques and remedies employed and by the care with which they were used. It was also interesting to observe the complete mutual confidence between the partners in the practice, which resulted in not ungenerous periods of leisure free from worry.

I fear, however, that your correspondent's pessimistic article will disuade some of those about to qualify from entering general practice.

Middlesex Hospital Medical School, London, W.1. J. D. WIGDAHL.

SIR,—Through his specialist glasses your correspondent sees too darkly the prospect of general practice. There is no doubt that the emphasis since the introduction of the National Health Service on the development of the hospital and specialist services, and the almost complete neglect of the general-practitioner services, have reacted to the disadvantage of general practice.

Let us remember, however, that one of the most important reasons for the National Health Service Act

was the tottering state of our domiciliary services, which in many ways were showing signs of severe strain. When after July, 1948, great numbers of people who previously could not afford a doctor of their own very naturally took advantage of their new-found opportunity, the situation in many areas became almost chaotic. Far from seeing the new situation as a revelation of the inadequacy of pre-service conditions, those unsympathetically inclined put the blame on the new service.

Even as at present constituted, the National Health Service presents an opportunity for raising general practice to the level already reached by the hospital and specialist services. This lies, I believe, in the development of group practice from health centres, for which the Act makes statutory provision. Unfortunately, just as Lord Dawson's original recommendation for health centres, put forward in 1920, was pigeon-holed because of economic pressure, so today health centres, although described by the Minister who introduced the Act as the keystone of our domiciliary service, have again, ostensibly for the same reason, been held up except for a few already being built. These few are very substantial buildings; but it does not seem unreasonable to suggest, with our lack of experience of how health centres can best function, that more temporary prefabricated structures, designed for adaptation to changing needs, might have better served the purpose of what is really a pilot study.

Group practice in health centres involves the coöperation of doctors, nurses, social workers, technicians, and other ancillary staff. This calls for coördinated action by the regional hospital board, local health authority, and local executive council, which are the administrative bodies concerned. At present no statutory body coördinates the activities of these three; and it seems very necessary in the interests of an efficient domiciliary service that there should be set up some such coördinating committee, called perhaps an area health service council.

While in many respects the Working Party's report is disappointing, its recommendations will go some way to redress the balance between the specialist and general-practitioner services. It is much to be regretted that its contribution to the establishment of group practice is so lukewarm.

For many reasons general practice today is far from being as good as we were promised, and as it could be under the terms of the National Health Service Act. Nevertheless, after 28 years' experience in a mostly industrial practice, I can confidently assert that the high standards to which your correspondent quite rightly aspires are more nearly attainable today than before the introduction of the service four years ago.

Edinburgh. S. LIPETZ.

SIR,—The time has really come when correspondents to the medical journals on matters concerning the National Health Service should appreciate the true facts. The letters which appear from week to week, if read by any uninformed person, must cause serious damage to the medical profession. The following statements are often found:

That doctors are inundated with clerical work and are thus unable to give proper attention to their patients.

Most of us have less clerical work than we had in the days of private practice. Sending out bills and recording and collecting fees was an onerous task that no longer exists. The keeping of records is no more than any doctor had to do for all his patients in the old days. Prescriptions have always had to be written, even for private patients.

That we have lost the freedom to practise that we had in the days before the National Health Service.

We are now at liberty—and it is a great advantage—to call on patients as often as they need without any consideration of whether they can afford it or not. Patients can be expected to visit us, rather than that we should be expected to visit them at their own convenience.

That we have lost the freedom of prescribing what we consider patients need.

Never were we able, in the past, to prescribe drugs regardless of their cost. In the days of private practice any doctor should have borne in mind the cost to the patient of expensive drugs. Any good doctor would have considered whether the high cost of a certain drug was justified by its clinical action. The less conscientious doctor considered that what the chemist received he lost.

That we have lost the freedom to sell the goodwill of our practices.

Most of us borrowed the money to buy a practice in the days before the war, and it took us very many years to repay the cost of purchase. Now, with income-tax at a high rate, no young man can ever expect to repay the purchase price of a practice. The freedom now bestowed on the incoming partner and the intaking partner must be felt personally to be realised.

The financial side of medical practice under inflation should also be realised. Because the pound is worth only half what it was before the war, the fees in private practice should be increased to twice what they were then. The experience of most general practitioners must be that, far from being able to double their fees, they find that most patients feel that they need a decrease if they are to remain as private patients.

Petworth, Sussex. W. A. BALL.

LEAD PAINT: A HAZARD TO CHILDREN

SIR,—I had intended on my return to this country to inquire about the known incidence of lead poisoning in children and to ask my clinical friends to bear in mind that it might be occurring. I was, therefore, most interested in the article on this subject by Dr. Millichap and his colleagues in your issue of Aug. 23.

The city of Baltimore, Maryland, has a population of 950,000. During the period 1931–51 there have been in that city 293 cases of lead poisoning in children, of which 83 have been fatal. The age-distribution of the 293 cases, with deaths of the 83 in parentheses, was: under 1 year, 19 (8); 2 years, 167 (51); 3 years, 67 (15); 4 years, 21 (3); 5 years, 11 (2); over 5 years, 8 (4).

Cases are still occurring, despite the efforts of the health department to warn parents not to allow their children to chew painted toys or paintwork on window-sills. There were 34 cases in 1949, 31 in 1950, and 20 in the first six months of 1951. The peak period is July and August.

A recent city ordinance has prohibited the use, for indoor painting, of paint unless it is free from any lead pigment; and a free service for the examination of blood for punctate basophilia is provided by the city health department.

ALLEN DALEY
Recently Associate Health Officer, Baltimore, Maryland.
London, W.14.

SIR,—Two children seen at this hospital in the past three months emphasise the plea made by Dr. Millichap and his colleagues for the recognition of the danger to young children in lead-containing paints. These cases also emphasise the need to consider the diagnosis of lead poisoning in children with vague cerebral symptoms, such as irritability and vomiting, and abnormal cerebro-spinal fluid.

Both patients, aged 3 years and 16 months, presented with irritability and vomiting, and a diagnosis of tuberculous meningitis was considered. Pallor was, however, marked in the second child, and, taken in conjunction with the cerebro-spinal fluid (C.S.F.) findings, suggested the diagnosis before more specific evidence was obtained. In both, the C.S.F. findings were typical of lead encephalopathy; lead lines were present in the bones; the punctate-basophil count was high (Lane's technique); and there was a high urinary-lead excretion. The first child is of special interest; for she was found to have a megaloblastic bone-marrow, and her case will be reported more fully in due course.

The source of lead in the first case is not yet definitely established, but the second child had ingested lead from the old and crumbling paintwork of an outside balcony. The lead content of the paint was 54% (calculated as the metal).

There is clearly a need for more safeguards against this danger than exist at present.

Whittington Hospital,
London, N.19. M. B. MORRIS.

ACTION OF ANTIBIOTICS

SIR,—I consider it dangerous to let your interesting leading article of Aug. 23 pass without comment, especially in so far as penicillin action is concerned.

That penicillin affects the assimilation of glutamic acid is beyond doubt, but it is equally beyond doubt that death of the cell does not come about because it has been deprived of the vital preformed glutamic acid. Many penicillin-sensitive staphylococci will grow without added glutamic acid and a *Bacillus subtilis* has been described which is extremely sensitive to penicillin, even when growing on a medium composed of inorganic salts and glucose only. Thus, we can have both penicillin-sensitive and penicillin-resistant organisms which are nutritionally independent of preformed glutamic acid or of any other amino acid. Dr. E. F. Gale, who has done such excellent work on this subject, has wisely avoided jumping to the easy conclusions which you expound. In spite of the tremendous amount of work done in the last few years on the mode of action of antibiotics, we are far from understanding how any of them works.

Wright-Fleming Institute of
Microbiology, St. Mary's Hospital
Medical School, London, W.2. DERRICK ROWLEY.

ATTENDANCE AT BOXING CONTESTS

SIR,—We are anxious to obtain the voluntary services of medical men to attend amateur boxing shows in London and the suburbs during the coming autumn and winter.

The shows usually take place in the evening, and the duties consist in examining the contestants (total time $^1/_2$–$^3/_4$ hour) and being available or on call for any serious injuries, which are usually very few. The only reward we can offer is a good boxing show and a convivial evening.

Medical officers will have the satisfaction of knowing that they are assisting to foster a high physical and moral standard in the health of the nation's youth.

Will doctors who are interested please write to me?

London Amateur Boxing Association,
69, Victoria Street, London, S.W.1. J. L. BLONSTEIN
Hon. Medical Officer.

BLOOD-PRESSURE ESTIMATIONS IN CHILDREN

SIR,—Your explanation (Aug. 16) that you were referring to research conditions in your leading article on the treatment of bacterial meningitis disposes at once of two of my objections to your proposed scheme of blood-pressure estimations—namely, that child manometer cuffs are not generally available, and that the suggested procedure would prove appallingly time-consuming. But not, I think, of my third, and perhaps most important, objection—that in most cases even when a reading has been obtained its value is doubtful.

The Waterhouse-Friderichsen syndrome occurs predominantly in young children, often very young children. Though desperately ill they are not, unless in the terminal stages, inert; on the contrary they are restless and resistive. They struggle against the manometer cuff and have to be firmly held. Of what value are readings obtained under such restraint? And are we justified in provoking these patients to expend their diminishing reserves of strength for the sake of such equivocal findings? By all means let us have as many accurate blood-pressure estimations as we can in coöperative patients; I agree that they afford valuable confirmatory evidence in diagnosis. But diagnosis is not so difficult as suggested, and, with respect, has seldom to be made from other very severe forms of ordinary meningitis, for in fact there is little similarity between the two conditions. The crucial feature of the Waterhouse-Friderichsen syndrome is that signs of meningitis are either extremely slight or, more usually, absent, and the conditions usually suggested to the clinician are malignant purpura or pneumonia.

Perhaps I can make my position clearer if I say that in my view any patient who presents with collapse and a purpuric or ecchymotic (*not* petechial) rash, particularly if there is livid cyanosis and perhaps polypnœa, should have a lumbar puncture. If this reveals an opalescent or turbid fluid under increased pressure, cortisone and sulphonamides should be given without delay; for this is one of the most acute emergencies in medicine—one has seen a patient die within 12 hours of taking ill. The amount of cortisone required is relatively negligible. I agree that its value in this syndrome should be most carefully assessed; but I submit that this has already been shown to be considerable; and if we are to wait until correct blood-pressure estimations have been made, then I submit, Sir, that many lives will be lost that might otherwise be saved.

South Middlesex Hospital,
Isleworth. G. E. BREEN.

CAROB FLOUR IN FUNCTIONAL VOMITING OF INFANTS

SIR,—Most babies who frequently vomit or regurgitate their food are just mild "posseters," but a few belong to the more serious and even alarming class of "habitual vomiters." These babies may reject their food any time within an hour of feeding. The trouble may start very soon after birth in either breast- or bottle-fed children. When an organic cause has been excluded, the diagnosis of "habitual vomiting" may reasonably be made. This is a functional disturbance of ingestion which includes cardio-œsophageal relaxation.[1] The problem of getting the baby to retain its food must then be tackled.

Most infants come to no harm from occasional or even quite regular vomiting, but the baby whose weight stays the same or actually falls is in danger, and under-nourishment may lead to dehydration and atrophy. And in spite of this the infant is hungry, alert, and avid for food which it cannot hold.

The usual treatment is to thicken the food by adding, say, wheat flour or arrowroot to the milk formula or to the expressed breast-milk, thereby increasing the viscosity of the milk and helping to keep it in the stomach. Phenobarbitone may also be given before each feed. These measures usually work in the simpler cases. Fine-oatmeal gruel and pureed potato made with milk are sometimes used, or the consistence of the feed may be suitably altered by using powdered or condensed milks, extra fluid being given as water between feeds. Whatever method is used there is an important disadvantage—the formula is poorly balanced for the infant's nutritional needs, and growth may be affected.

It was with much relief that I heard of Professor Lelong's work in Paris on this problem. All degrees of persistent functional emesis in infants were treated with milk thickened by the addition of carob flour, a powder extracted from the seed of the Levantine carob tree. Information about this legume, *Ceratonia siliqua* (Linne), is given by Glanzmann.[2] This flour was prepared for Professor Lelong's trials by the Nestlé Company of Switzerland, and has proved indispensable. Its virtues are that it has no flavour, it thickens the milk without lessening its digestibility or changing its nutritive value, and it is completely inert and neutral. But it does alter

1. Neuhauser, E. B. D., Berenberg, W. *Radiology*, 1947, **48**, 480.
2. Glanzmann, E. Einführung in die Kinderheilkunde. Vienna, 1949; p. 220.

the consistence of the feed so that it is rare for even a severe case not to respond satisfactorily.

0·5–2% (usually 1%) of the powder is added to each feed—i.e., one measure to 100 ml. (3 ounces) of cold breast, ordinary, or modified milk. Any sugar and water required is added to this mixture, and the whole is brought to the boil. When powdered or condensed (evaporated) milk is used, the powder is mixed with the necessary water, and the mixture brought to the boil for a moment before the milk is added with vigorous beating.

Carob flour is available on the Continent and is widely used in Switzerland, France, and Belgium. In this country the powder, which is marketed abroad under the trade name of 'Nestargel,' has received only one mention as far as I know; Evans and Mac Keith[3] say: "The addition of ½–1% of 'Poudre Épaississante Nestlé' Nestargel to the feed makes it so adhesive that the child cannot vomit it, but this preparation is as yet not generally obtainable."

The import of carob flour for sale in the United Kingdom is forbidden, and the flour which I have myself used was kindly supplied by the Nestlé Company. I have only been able to try it so far in nine cases, but all these have been severe enough to resist all routine measures. All nine babies were cured or remarkably improved in a very short time, all within two weeks and the majority within a week. The mothers were given the powder with instructions on its use, and they had no difficulty in preparing the feeds.

I have no doubt of the efficacy of carob flour in this condition. Its value deserves to be widely known, and the flour should be readily obtainable. I would go so far as to say that if there is no improvement after its use, the diagnosis of the cause of vomiting must be suspect. Before others can share my enthusiasm, the ban on the sale of carob flour in Britain must be lifted.

Dr. Helen Morley kindly provided me with several of the patients in my small series.

Duchess of York Hospital for Babies, Manchester. THEODORE JAMES.

NURSES IN THE MAKING

SIR,—Mr. Hodkinson's letter[4] has been followed by a leading article in your issue of Aug. 9.

My experience of a cadet scheme in this mental-deficiency hospital appears to run parallel to that of Mr. Hodkinson, even to the intention not to publicise it until more experience had been gained. The scheme has now been running for nearly 3 years, and results hitherto have been wholly satisfactory.

Two whole days a week are spent in school on "further education" with a teacher provided by the local authority. Three half-days a week are devoted, under the supervision of our nurse-training school, to subjects which will lead up to the preliminary State examination; and three half-days are spent in the various departments of the hospital. These young people are at no time regarded as nurses, and their status in the hospital is that of a student; association with all but the youngest patients is minimal, and regulations regarding the employment of young persons are strictly adhered to, although in view of the student status of the cadets these regulations rarely apply.

Mr. Hodkinson lists five advantages and five essential features. I have just looked up one of my earlier reports on our cadet scheme, and find that I came to the same conclusions, in almost the same order and the same words. If I had to select one outstanding element in the success of any cadet scheme, I would say that this is the "student" as opposed to the "employee" status of the cadet; and I would add that in this hospital we accent the "career" element in nursing, as opposed to the "vocation." All young people on application are medically examined and educationally and psychologically tested; and we believe that the young men or women who tell us that they wish to take up nursing because the career seems interesting, the money is good, and they wish some day to be a chief male nurse or matron, are better candidates than those who claim they have a call to do nursing. On inquiry this too often is found to mean that they have a call for nothing and that they are just drifting into nursing and will thus probably drift out again.

The cadet scheme in this hospital is practically our only source of student-nurse recruitment; it has saved the nurse-training school from extinction and the hospital from the closure of beds.

The raising of the minimum age for student nurses to 18 years is a blow to nurse recruitment, but not, I think, too serious a blow; it will dam but will not choke the stream.

Your statement that "there are good arguments for the view that whatever a girl does between leaving school and starting her nursing training, at least she should keep clear of hospitals" is a denial of the fact that some hospitals can lay themselves out to ensure that everything that can be done is done to provide for the proper mental, physical, and emotional maturation of the young male or female nursing cadet.

I believe that properly run cadet schemes, run on "further education" lines, are the answer to the nursing shortage. I also believe that badly run schemes are likely to cause much harm to nursing recruitment.

Prudhoe and Monkton Hospital, Prudhoe-on-Tyne, Northumberland. GEORGE MCCOULL.

INCISION FOR APPENDICECTOMY

SIR,—I was very interested in Mr. Young's account (Aug. 9) of his method of extending Battle's incision where pelvic or other disorders are unexpectedly encountered.

I have used in about a hundred cases a method which, for want of a better name, I call the "transverse retro-rectal approach," and which also may be extended if necessary.

An incision is made in the plane between the anterior superior spines of the ilium. Starting in the midline and extending to the right over the right rectus abdominis muscle, it may be made in the natural crease which often lies at this level. The rectus sheath is opened in the same direction as the skin incision; the rectus muscle is freed from its sheath posteriorly by stripping it with the index fingers, and the muscle is retracted medially. The posterior lamella of the rectus sheath with the closely adherent transversalis fascia and peritoneum is picked up above the level of the linea semicircularis and opened transversely: care must be taken not to include the gut, which is closely applied to the peritoneum here. The inferior epigastric artery, which has just entered the sheath across the linea semicircularis, is medial; it is usually adherent to the rectus muscle and is retracted with it.

If a pelvic or abdominal condition requiring a more extensive exposure be encountered the approach may be converted into a Pfannenstiel by extending the skin incision transversely to the left over the left rectus muscle, opening the left rectus sheath in the line of the skin incision, separating and retracting laterally the recti muscles, and extending the previous opening behind the right rectus transversely behind the left rectus. It is, of course, possible to extend the incision to the right by cutting through or separating the oblique and transversus muscles as in Weir's approach.

The advantages of the approach are that it is adequate, and the pelvic organs can be easily examined; and the incision can be extended without damage to nerves and, possibly, consequent hernia. Wound healing is earlier; sutures may be removed on the fifth day. The scar is thin, strong, and almost invisible. Keloid formation is rare—possibly because the incision lies in the natural

3. Evans, P. R., Mac Keith, R. Infant Feeding and Feeding Difficulties. London, 1951.
4. Hodkinson, S. *Lancet*, 1952, i, 1113.

skin-tension lines of Langer. The scar does not tend to stretch, and as it is transverse and often in the crease line it is cosmetically satisfactory.

River Hospitals,
Joyce Green,
Dartford, Kent.

JOHN MCDONALD.

HYPOGLYCÆMIA IN ROAD USERS

SIR,—Motor accidents have very rarely occurred because of hypoglycæmia in diabetics who are taking insulin. This condition may arise from several causes, such as omitting to eat the necessary carbohydrate at the usual time—i.e., at breakfast, in the middle of the morning, at the midday meal, at tea-time, or at the evening meal. If the carbohydrate is either omitted or delayed, a severe reaction may occur owing to unopposed overaction of the insulin. A hypoglycæmic attack may also be produced by taking unusual exercise shortly before the car is driven, or as a result of changing a wheel.

The medical advisory committee of the Diabetic Association therefore asks all doctors looking after diabetics taking insulin and driving motor-cars, or riding motor or pedal cycles, to make certain that their patients understand the possible causes of hypoglycæmic attacks and how they can be prevented by regular intake of carbohydrate at the usual meals, which should be taken punctually. Some extra carbohydrate should be eaten both before and after any unusual exercise. A supply of biscuits or 12 lumps of sugar or glucose should always be carried in the car or cycle in case a meal is unavoidably delayed, or unexpected exercise is necessary.

The committee especially hopes that, if a doctor knows that a patient sometimes does not recognise the symptoms of hypoglycæmia, he will advise his patient not to apply for a driving licence.

Diabetic Association,
152, Harley Street,
London, W.1.

R. D. LAWRENCE
Chairman,
Medical Advisory Committee.

FLUORINE INTAKE IN BRITAIN

SIR,—The decrease in the incidence and spread of dental caries in certain townships in the United States, resulting from the fluoridation of communal drinking-waters, has led to the suggestion that fluorine should be added to British public water-supplies at a concentration of one part per million which, together with the ingestion of fluorine in ordinary food, would put the total daily fluorine intake at about 2·20 mg.[1 2] Subsequently a basic ethical objection to such compusory mass medication was made on behalf of the League of British Housewives.[3]

Considerations of the real differences in nutrition and distribution of population between different countries appear to have been neglected by those responsible for the suggested fluoridation of water-supplies. Small amounts of fluorine occur naturally in many sources of British drinking-waters; but fluorine-containing ores, fluxes, and coals are now used industrially in this country in large quantities. Fluorine compounds are toxic when inspired or ingested; and, since they may be encountered in various ways in industrial processes, they present a definite hazard to the health of man and animals. Animal fluorosis is being increasingly noted by British farmers and veterinary officers, especially in the neighbourhood of iron and steel works and of coal-consuming electric power stations.

Animals can be moved from contaminated pasture, but human beings remain in a polluted atmosphere. The etching of window glass by hydrofluoric acid—an easily recognised sign of atmospheric pollution—is now seen in industrial homes; and in these contaminated regions, examination of the teeth of children and estimation of urinary fluorine in adults gives evidence of the absorption of fluorine in excess of that known to come from the local drinking-water.

In a healthy man a fluorine intake of up to 5 mg. daily can be eliminated, but above this level there is retention of fluorine in the body with cumulative effects in bone.[4] A recent investigation[5] has described the effects of chronic fluorosis on kidney structure and function in rats, with a view to demonstrating the existence of a fluorine hazard before such severe intoxication has resulted as to cause obvious skeletal lesions; the histological examination indicated that in the kidneys there was vascular, glomerular, and more obviously tubular, dégeneration leading to interstitial fibrosis.

We do not know how high the actual intake of fluorine is at present in the various industrial regions of this country, and, until further inquiry is undertaken with regard to the fluorine hazards to which different neighbourhoods are now exposed, it seems most undesirable that fluorine should be added to public water-supplies in Britain.

Laboratory of Human Nutrition,
University of Oxford.

DAGMAR WILSON.

BONE REGENERATION

SIR,—Following your survey of this subject (Aug. 23) I should like to refer to recent work on bone grafts carried out in this department by Mr. John Hutchison.[6]

Bone autografts and homografts were implanted into bone, muscle, and the anterior chamber of the eye of rabbits, and their histological progress followed and compared from 10 to 180 days. Hutchison's findings are in many respects contrary to those recorded by Barth[7] and Reynolds and Oliver[8] to which you referred. Even at an early stage (10–21 days) there is a striking difference in the histological appearance of autografts and homografts. In the bone autograft, while the osteocytes, more particularly the centrally situated cells, die, the soft-tissue elements of the graft—periosteum, lining of Haversian canals, and endosteum—show active cellular proliferation and are responsible for the subsequent cellular repopulation of the graft which is complete after 40 days. The bony matrix retains its staining affinity, and by 42 days the picture is that of active living bone with no evidence of any dead bone, as implied in your article.

The autograft at 42 days therefore represents bone formed by the original cell elements of the graft and may well include much of the original bony matrix of the graft. As these cells constitute the essential living part of bone and are largely responsible for the new bone formation it is evident that the autografts survive. The period required for complete recovery varies according to the type of graft, and is naturally longer in dense cortical grafts. By contrast, sections of the bone homografts from 10 days onwards show typical dead bone with empty lacunæ and faintly stained opaque matrix—the classical sequestrum. There is, with an odd exception, no absorption of the dead homografts, which can be recovered 180 days after implantation.

Hutchison's findings correspond to those recently recorded in an experimental study by Ray et al.[9] Ham[10] has also noted the osteogenic activity of the surviving cells of bone autografts.

Both heterotopic bone autografts and homografts induced active osteogenesis by the connective tissue of the host from 10 to 42 days, which then ceased. In the case of homografts this new bone formed by the host tissue died after 42 days and was added to the graft

1. Mackenzie, E. F. W. *Lancet*, 1952, i, 961.
2. *Ibid*, 1951, i, 1356.
3. Sykes, W. M. *Ibid*, 1952, i, 1112; *Ibid*, Aug. 2, 1952, p. 242.
4. McClure, F. J., Mitchell, H. H., Hamilton, T. S., Kinser, C. A. *J. industr. Hyg.* 1945, **27**, 159.
5. Bond, A. M., Murray, M. M. *Brit. J. exp. Path.* 1952, **33**, 168.
6. Hutchison, J. *Brit. J. Surg.* 1952, **39**, 552.
7. Barth, A. *Arch. klin. Chir.* 1893, **46**, 409.
8. Reynolds, F. C., Oliver, D. K. *J. Bone Jt Surg.* 1950, **32A**, 283.
9. Ray, R. D., Degge, J., Gloyd, P., Mooney, G. *Ibid*, 1952, **34A**, 638.
10. Ham, A. W. *Ibid*, p. 701.

sequestrum. Unlike Urist and McLean,[11] Hutchison found little evidence of host osteogenesis in intra-ocular transplants of bone autografts or homografts, and he concluded that this was due to the absence of marked tissue reaction. Ham is of the opinion that osteogenesis following implantation of bone grafts into muscle is entirely due to the surviving cells of the graft, and not to metaplasia of host connective-tissue cells. While this is not the generally accepted view, it would explain the death of the new bone formed around the implanted bone homograft.

Thus the behaviour of bone grafts in a general way resembles that of other tissue grafts—autografts survive and homografts die (except, of course, cornea and cartilage). The more critical initial test period before the bone autograft "takes" is to be expected because of the difficulty in vascularisation.

Department of Anatomy,
University of Glasgow. G. M. WYBURN.

FEEDING DISORDERS IN INFANTS

SIR,—In his comments (Aug. 16) on Sister Morrison's letter, Dr. Wood introduces a new theme—the advice given in the lay press—possibly because he happens to know that this is the medium for Sister Morrison's work.

She would not wish to reply about the success of her own work, but I think it should be known that mothers constantly write back that after they have followed her advice their babies are contented and progressing well. So far from being "baffled," the mothers are given a sense of reassurance and confidence.

Why should it be doubted that writers for the lay press have just as keen a sense of responsibility—and just the same range of opinion—as other members of their professions? And seeing their advice in type gives them the incentive, and the opportunity, to make it as clear as possible.

Nursery World,
154, Fleet Street,
London, E.C.4. MADELEINE POTTENGER.

BOOKS ON HOSPITALS

SIR,—I beg leave to supplement your correspondent's contribution (Aug. 23) on this subject with the titles of a few excellent publications he has omitted.

The functional evolution and the geographical distribution of early English hospitals is well described in *The Medieval Hospitals of England* by Mary Clay (1909), and in *Houses of Pity* by J. E. Hobson (1926). Two hundred years' history of Dublin's Rotunda Hospital has been recently recorded in two books which were reviewed in your columns.[12] In the same week the *British Medical Journal* published an interesting brief account[13] of the seven centuries' history of Europe's first mental hospital—the Bethlem Royal.

There are also two small books well worth reading which deal with the history and management of most of London's non-teaching hospitals. *The Metropolitan Asylums Board and its Work 1867–1930*, written by Sir Allan Powell, was published by the Board in 1930 and describes the vicissitudes of its 44 fever, mental, tuberculosis, children's, and special hospitals with 24,000 beds. *The L.C.C. Hospitals—a Retrospect* was published by the London County Council in 1949, and carries forward the history of 98 of London's "poor-law" and municipal hospitals with 72,000 beds from 1930 to 1948.

The Ministry of Health, which now controls most of the hospitals in England and Wales, has an unrivalled opportunity, which it should not miss, to produce the most up-to-date book on the hospital history of this country.

London, S.E.1. WILLIAM HARTSTON.

11. Urist, M. R., McLean, F. C. *Ibid*, p. 443.
12. Curran, C. P. The Rotunda Hospital—Its Architects and Craftsmen. Dublin, 1946. Browne, O'D. T. D. The Rotunda Hospital, 1745–1945. Edinburgh, 1947. See *Lancet*, 1947, i, 916.
13. *Brit. med. J.* 1947, i, 935.

TREATMENT OF PULMONARY TUBERCULOSIS

SIR,—The symposium in your issue of Aug. 23 makes it clear that the treatment of pulmonary tuberculosis at Clare Hall Hospital is based on very sound principles.

There may be disagreement, however, with one of Dr. Macdonald's observations on the use of artificial pneumothorax. He says: "We hesitate to do a pneumothorax . . . of course . . . if there is too little disease." This hesitation would appear to originate in a wish to avoid serious complications, or possibly in a suspicion that the procedure might be unnecessary. But empyema, fistula, and inexpansible lung usually result from the use of pneumothorax treatment in unsuitable cases.[1] When the disease is minimal ("too little"), such complications need not ordinarily be expected. The observed prognosis of minimal pulmonary tuberculosis is not good, between 20% and 80% of cases showing progression during the first 2–3 years after diagnosis.[2–8] Early collapse therapy can improve the prognosis.[9–11] Therefore, neither of the presumed objections to the use of pneumothorax in minimal disease seems valid.

Many patients with minimal tuberculosis are now referred to the chest clinics from mass-radiography units. Adolescents and young adults form the majority of such cases. Progression of disease can be expected in a high percentage of these young people. Their supervision commonly consists in the inspection of serial radiographs taken at intervals of 3 to 6 months. But diffuse bronchogenic spread and cavitation during the intervening months is seen all too often. The advantage of early diagnosis is then lost. Any minimal disease which has shown the slightest tendency to progress whilst closely observed is probably one of "the positive criteria for inducing a pneumothorax" which your leading article seeks.

Poole Sanatorium, Nunthorpe,
nr. Middlesbrough. J. P. ANDERSON.

SIR,—The excellent article by Dr. Simmonds and his colleagues interested and instructed me. I was, however, pained to note the reference to "resection-minded Liverpool." I thought this bogy had been well and truly laid by Coope, but apparently it has to be done again.

There are in Liverpool a number of thoracic surgeons operating at various hospitals in coöperation with chest physicians. The number of different views on tuberculosis and its treatment is probably equal to the number of surgeons or the number of institutions concerned, whichever is the greater. F. R. Edwards and his associates, working at Aintree Hospital, have pushed the indications for resection much further than most people; but, as far as I am aware, they have never claimed that this is anything but a large-scale experiment. Other thoracic surgeons in Liverpool, in common with those in the rest of the country, will await the analysis of their cases and the 5-year follow-up figures with considerable interest, and possibly radical consequences to their future policy in treating pulmonary tuberculosis. Meanwhile, Liverpool remains a geographical area where all forms of treatment for pulmonary tuberculosis are practised, and each case is considered on its merits and the form of treatment is advised that is most likely to ensure success in the particular circumstances.

1. Mitchell, R. S. *Amer. Rev. Tuberc.* 1951, **64**, 141.
2. Zacks, D. *Ibid*, 1939, **39**, 683.
3. Simon, G. *Brit. J. Radiol.* 1943, **16**, 217.
4. Brooks, W. D. W. *Lancet*, 1944, i, 745.
5. Bobrowitz, I. D., Hurst, A., Martin, M. *Amer. Rev. Tuberc.* 1947, **56**, 110.
6. Tuberculosis in Young Adults: Prophit Tuberculosis Survey. London, 1948.
7. Chang, R. *Amer. Rev. Tuberc.* 1948, **58**, 610.
8. Aspin, J. *Tubercle*, 1949, **30**, 8.
9. Wingfield, R. C., Macpherson, A. M. G. *Brit. med. J.* 1936, i, 741.
10. Amberson, J. B. Cited in Prophit Tuberculosis Survey. London, 1938; p. 171.
11. Paine, A. L. *Amer. Rev. Tuberc.* 1951, **63**, 644.

I myself find it increasingly embarrassing to have to explain to visitors and colleagues that I meet that I am in no immediate danger of forgetting how to do a thoracoplasty or an adhesion division. A general surgeon accused of being "cholecystectomy-minded" would rightly take this as a reflection on his professional judgment. The suggestion of being "anything-minded" implies that prejudice or obsession has taken the place of scientific judgment. May I please put it on record that this is not the case in Liverpool.

Liverpool. LESLIE J. TEMPLE.

MEGALOBLASTIC ANÆMIA OF PREGNANCY

SIR,—In your issue of Aug. 2 Dr. Israëls and Dr. Da Cunha emphasise the importance of early diagnosis in megaloblastic anæmia of pregnancy, as this disease is not at all rare and can be adequately treated. They state that folic acid remains the treatment of choice, because vitamin B_{12} has been found ineffective against this condition in temperate climates.

We have previously described [1] a case of megaloblastic anæmia in the puerperium reacting to vitamin B_{12}. In this case analysis of the gastric juice showed the presence of free HCl. This excluded the possibility of addisonian pernicious anæmia. Determination of the fat content of the fæces (total fat 50% of the dry weight) pointed to non-tropical sprue. We came to the conclusion that megaloblastic anæmia in pregnancy in the temperate zone may be classified as: (1) addisonian pernicious anæmia, (2) non-tropical sprue, and (3) true megaloblastic anæmia of pregnancy or puerperium.

Since then we have seen a patient of 23, primigravida. She was examined in November, 1950. Her hæmoglobin was then 12·5 g. per 100 ml. In April, 1951, she was admitted to hospital because of severe anæmia, which progressed while she was treated with iron.

The patient was 8 months pregnant. She complained of dyspnœa on exertion, headache, and œdema. She suffered from vomiting, which had improved during the last 2 or 3 weeks. Examination showed a systolic murmur. Liver and spleen were not palpable. The tongue was normal. No signs of polyneuritis or involvement of the central nervous system.

Investigations.—Hb 5·4 g. per 100 ml.; red blood-cells 1,200,000 per c.mm.; white blood-cells 10,000 per c.mm.; smear of peripheral blood showed 14 nucleated red cells (including some megaloblasts) per 100 white cells. Bone-marrow: hyperplastic, megaloblastic.

Fractional gastric analysis (free and total acidity in ml. of 0·1 *N* HCl per 100 ml.): (1) 0/27, (2) 0/5, (3) 0/7, (4) 0/12; after histamine (5) 6/6, (6) 14/30, (7) 28/45, (8) 34/48.

Serum-iron 370 µg. per 100 ml.; blood-bilirubin 0·6 mg. per 100 ml.

Fæces over a 3-day period on a Schmidt's diet: total weight 110 g.; dry weight 30·5% of total weight; total fat 29% of the dry weight.

Glucose-tolerance curve: fasting, 79 mg. per 100 ml., 30 min. 174 mg., 60 min. 149 mg., 90 min. 73 mg., 120 min. 65 mg., 150 min. 74 mg.

Treatment.—She was given 400 ml. of blood, which raised her Hb to 6·2 g. per 100 ml., her red-cell count to 1,500,000 per c.mm., and the hæmatocrit volume to 22·1%. Treatment with vitamin B_{12} was started on April 18; 15 µg. daily was given by injection for three days. On the third day she felt better, and the subjective improvement continued. It was accompanied by a reticulocyte crisis of 17·3% on the ninth day. On May 2 her Hb was 9·07 g. per 100 ml., red cells 2,180,000, and hæmatocrit volume 30%. Vitamin B_{12} was again given (15 µg. every other day) until May 13, when she was delivered of a healthy child.

Blood examination on Jan. 18, 1952, showed Hb 12·8 g. per 100 ml., and red cells 4,710,000 per c.mm.

In this case the normal fat content of the fæces and the normal glucose-tolerance curve excluded the possibility of non-tropical sprue, while the presence of free HCl after histamine is strongly against the diagnosis of addisonian pernicious anæmia.

1. Nieweg, H. O., van Buchem, F. S. P., Stenfert Kroese, W. F. *Acta med. scand.* 1952, **142**, 45.

At the University of Utrecht medical clinic Verloop [2] observed the effectiveness of vitamin B_{12} in similar patients. In the Netherlands at least, there are two groups of megaloblastic anæmia of pregnancy: the first is caused by a deficiency of vitamin B_{12}; and the second by a lack of folic acid. This differentiation is, of course, of practical importance because of the danger of neurological lesions in patients with vitamin-B_{12} deficiency who are given folic acid.

University of Groningen, Holland. H. O. NIEWEG.

ACHALASIA *v.* CARDIOSPASM

SIR,—Hurst is dead: otherwise he would have replied to your peripatetic correspondent's attack (Aug. 16). Hurst gave up many of the concepts and therapies mentioned long before his death. "The absent acid-barrier in pernicious anæmia" was forgotten in 1928, although I well remember in 1930 Castle, who attended one of Hurst's combined rounds, saying with obvious sincerity that if Hurst had not emphasised the absence of acid and published his supposedly cured case of Addisonian anæmia, he (Castle) would never have thought of doing his experiment of predigesting a steak in a healthy stomach and transferring it to a patient with Addisonian anæmia.

Though Hurst gave up his views about catarrhal jaundice, somewhat obstinately, he never gave up the concept of achalasia. When I do a rectal examination in a patient, if he has a fistula, a fissure, or a thrombosed pile, the sphincter sometimes goes into spasm and this I call anal spasm. In people with a healthy lower gut, the finger usually slips in easily—i.e., there is complete "chalasia." Hurst constantly pointed out that when the mercury tube (I cannot remember his miscalling it a "bougie") passed into the stomach as the sphincter relaxed, the tube was not gripped as it would be in cardiospasm. It was this observation which made him ask Sir Cooper Perry "for a single word to express 'absence of relaxation.'"

This observation I confirmed this morning when I visited a patient who in the past twenty years has passed her tube over 3000 times. This woman of 53 kindly passed her tube while I waited in the next room, and I was able forthwith to show that there was no gripping, or, as she said: "When the tube passes the obstruction, which is rather difficult, there is no difficulty in withdrawing it." She, however, usually keeps it down for five minutes, and she has discovered that this suffices for two to three days of easy swallowing. She has also discovered that it helps to have had a light meal.

Your peripatetic correspondent says that Douthwaite congratulates Avery Jones on excluding "the inept word from his new book." But Avery Jones has not done so. Two of his authors, both surgeons, write thus:

Ronald Belsey (p. 156) says in the differential diagnosis of hiatus hernia from "Achalasia of the cardia. Dilatation of the œsophagus is rare in hiatus hernia, even with stenosis and usual in achalasia. The symptoms are different and the response to octyl nitrite is diagnostic of achalasia"; and Geoffrey Wooller (pp. 179–199) gives achalasia as a synonym for cardiospasm but uses the word cardiospasm "in the belief that spasm of the cardia exists in the majority of patients," although he admits: "The cause of cardiospasm is unknown. Psychogenic trauma is an important factor in initiating its onset."

I am grateful to your peripatetic correspondent for making me do a little research, and rather than try to decry Hurst's work and his disciples as he does I would like to suggest that we get more information on two unsettled points.

Firstly, several people doubt Geoffrey Rake's work,[3] confirmed by E. A. Gallinaro,[4] that achalasia is caused by degeneration of Auerbach's plexus and think this is the effect rather than the cause. Surely it is possible to examine Auerbach's plexus in patients dying from other

2. Verloop, M. C. Personal communication.
3. *Guy's Hosp. Rep.* 1926, **76**, 145; *Ibid*, 1927, **77**, 141.
4. *Rass. Neurol. veg.* 1947, **4**, 464.

forms of prolonged obstruction to settle this point, which has been in doubt for twenty-five years.

Secondly, believing as I do that achalasia is curable by Hurst's mercury tube, the passage of which I admit is unpleasant to many people and well-nigh impossible for children, can we get some idea how often it must be passed? Psychology plays its part, and I remember how forcefully that was impressed on me in 1924 when as a ward clerk I sat at John Ryle's feet.

An outpatient, a boy of some eighteen years, on being asked how his achalasia was, said he was much better, had gained in weight, could swallow well, &c. Ryle, not realising that the boy had not finished, pointed out to us how Dr. Hurst had invented this tube and what great advantage the boy had received. Thereupon the boy said he had really come up to say that he had not passed the tube for some weeks when, at a religious meeting, he had received the laying-on of hands. John Ryle immediately said that was the type of discipline so good for us.

Unfortunately I cannot tell the end of the story, but G. Wooller in Avery Jones's book *Modern Trends in Gastroenterology* records instances of "cardiospasm" occurring after psychological trauma, and I am sure there are other "cures" such as the one recorded above. Until we know this we cannot really judge the value of surgical treatment; we should also know more about the asymptomatic patients—one of whom I know, besides being the headmaster of a public school, is also a distinguished athlete. I feel that Hurst if he were alive would be the standard-bearer of surgeons who operate successfully on this condition; but he lived in the age of "cardioplasy, œsophagoplasty and œsophagogastrostomy" which, as Wooller says, "are killing operations"; and even though Hurst persuaded surgeons to operate, they approached the cardia abdominally, and so had no real successes.

If I have written in a partisan manner it is because, as John Ryle said in the introduction to Hurst's autobiography: "To know Hurst and his enthusiasms, his generosity, his courage and his foibles, was an education in itself. All who worked with him regarded him with admiration and affection." Nevertheless medicine demands the most rigid disciplines and so, casting aside personal considerations, I say my strongest conviction is that the commonest cause of "idiopathic" enlargement and dilatation of the œsophagus is failure of the cardiac sphincter to relax, and this syndrome merits the word "achalasia."

Rugby. R. E. SMITH.

CHLOROPHYLL AS DEODORANT

SIR,—The phrase "as dark as the inside of a cow" is traditional, and it is probable that our own insides are about equally dark though this does not have the authority of tradition. Photosynthesis, as the name implies, depends on light, and it is only after illumination that chlorophyll-containing systems are able to bring about the reaction between carbon dioxide and water that releases oxygen. Your suggestion (Aug. 23) that the alleged deodorising action of chlorophyll could be due to oxygen formation seems therefore a little improbable. Furthermore this action has not yet been brought about by isolated chlorophyll but only by fairly fresh chloroplast preparations.

But an explanation of the phenomenon might well be postponed until it is certain that there is a phenomenon to explain. Can no-one produce a statistically significant number of "second-best friends" on whom a proper experiment could be tried?

Rothamsted Experimental Station, Harpenden, Herts. N. W. PIRIE.

SIR,—In your leading article you reproduce from the *News Chronicle* of July 30 a couplet to the effect that goats, in spite of the fact that they feed all day long on chlorophyll, tend to be odorous.

Whilst we are not disputing this fact, we would remark that only water-soluble derivatives have been used as deodorants. Chlorophyll, as found in nature, is not water-soluble and it has to be specially processed in order to render it so. All the claims concerning the deodorant properties of chlorophyll have been based on this water-soluble variety.

Ashe Laboratories Ltd., Leatherhead. L. DEADMAN, Chief chemist.

FUNCTIONAL DISORDERS OF THE SMALL INTESTINE

SIR,—With the increasing advocacy of the operation of partial gastrectomy in this country, functional disorders of the small intestine seem likely to become of importance, and it is good to see Dr. Morton Gill and Dr. Falle drawing attention to them in their article (Aug. 2).

In some people partial gastrectomy appears to uncover a latent tendency to a small-gut motility disturbance; in others the functional disorder undoubtedly precedes the formation of a peptic ulcer and is present before gastrectomy. In these unfortunates disastrous results are inevitable; it behoves us to make sure before recommending operation that the motor function of the small gut is stable, especially if the patient is a woman.

Harrogate. A. J. GLAZEBROOK.

Obituary

JOHN GEOFFREY CUTTS
M.R.C.S.

Dr. Geoffrey Cutts, medical officer to the Northwood, Pinner and District Hospital, died in London on Aug. 18, from poliomyelitis, at the age of 37.

He was educated at Oakham in Rutlandshire, and at St. Mary's Hospital, where he qualified in 1940. After holding house-appointments elsewhere, he returned to St. Mary's as resident anæsthetist in 1942, and the following year he was appointed house-surgeon to the surgical unit at Harefield Chest Hospital. In 1944 he joined the Royal Navy, and he served as E.N.T. specialist in H.M. Hospital Ship *Tjitjilengka* in the Far East. At the end of the war he joined an old-established firm of general practitioners in Hatch End, and was soon appointed to the staff of Northwood Hospital.

W. R. writes: "Northwood Hospital is one of those centres where general practitioners work together as a happy team and, thanks to his early training in anæsthetics and E.N.T. work, Cutts proved himself a most accomplished specialist in both those departments. Not a man to be hurried, he showed dignity and a steady approach to his work. A little shy, slightly stubborn, he never jumped to hasty conclusions or reached a decision without careful thought. The best time to see him was at a difficult obstetric case. It is there that patience may be a supreme gift, and Geoffrey Cutts possessed it more than most of us. In the last few years of difficulty and transition he acted as secretary to the medical staff with conspicuous success. Good general practitioners are not born every day, and we have lost one of the best of them at a tragically early age."

Dr. Cutts leaves a widow and two young children.

Births, Marriages, and Deaths

BIRTHS

GOLD.—On Aug. 28, at South Hill Farm, Eastcote, Pinner, to Betty wife of Dr. Stephen Gold—a son.

HARDMAN.—On Aug. 28, at the Churchill Hospital, Oxford, to Philippa (née Woolf), wife of Dr. Maurice Hardman—a son.

WOLFE.—On Aug. 30, at University College Hospital, London, W.C.1, to Lesley (née Fox), wife of Mr. H. R. I. Wolfe, M.S., F.R.C.S.—a son.

DEATHS

HUNNARD.—On Aug. 30, at Dulwich Wood Avenue, London, S.E.19, Arthur Hunnard, M.B. Lond., aged 81.

HUNTER.—On Aug. 27, Charles Stewart Hunter, L.R.C.P.E., D.P.H., F.R.S.E., of 12, Becmead Avenue, Streatham, S.W.16, late of Darvel and Carnoustie.

STEPHENSON.—On Aug. 26, at West Haddon, William Arthur Stephenson, M.R.C.S., aged 84.

Notes and News

CAPITAL EXPENDITURE ON HOSPITALS

IN calling on hospital authorities to submit capital estimates for 1953–54, the Ministry of Health announces (R.H.B. [52] 97) adjustment of the previous formula, particularly to help those regions where the need seems to be greatest. Boards are to submit estimates, within their allocations, which are to be in gross figures of which boards will be authorised to spend 80% during the year. The additional percentage has been included to allow greater flexibility within the programme. The following are the allocations to regional boards in 1953–54:

Region	*£000*
Newcastle upon Tyne	526
Leeds	475
Sheffield	721
East Anglia	248
North-west Metropolitan	600
North-east Metropolitan	468
South-east Metropolitan	499
South-west Metropolitan	787
Oxford	235
South Western	429
Birmingham	715
Manchester	681
Liverpool	325
Welsh	478

To boards of governors the allocation will be in the range of £40,000–80,000 for undergraduate teaching hospitals and of £10,000–35,000 for postgraduate teaching hospitals.

Boards are to assume that the allocation for 1954–55 will not be greater than that in 1953–54. The Ministry draws attention to the urgent need to increase the provision for mentally ill and mentally defective patients. It also suggests that boards, in planning their capital programme, should have particular regard for works which may bring about some decrease in maintenance costs. The Ministry will continue to make special provision from a central reserve for certain large schemes that are now being carried out.

SENIOR REGISTRARS IN THE NORTH-WEST METROPOLITAN REGION

ACCORDING to the Ministry of Health's revised allocation, this region is to have substantially fewer senior registrars than at present. The regional hospital board has accordingly been considering how they can most fairly cut their coat to fit their cloth. They have decided to give notice to all the senior registrars now under contract with them, to take effect on March 31, 1953. Before that date the reduced number of posts will be readvertised and all the present senior registrars will be free to apply for them.

The board also proposes to appoint a number of "assistant physicians" and "assistant surgeons."

The holder of one of these posts will have the status of consultant and be on the consultant salary scale, but he will be attached to a particular firm. He will have his own beds but the general scope of his responsibility will be outlined by the head of the firm. The appointment will be on a whole-time basis for five years with the option of transferring to a part-time appointment for the maximum number of sessions at the end of that period.

The senior administrative officer assured the board that he had received from the chairman of the Joint Committee of Consultants and Specialists and the Royal Colleges a verbal assurance that these proposals were acceptable to them.

The board has agreed to a proposal made by the board of governors of St. Mary's Hospital for an interchange of senior registrars, between selected regional hospitals and St. Mary's Hospital. For the present it is suggested that six senior registrars in medicine and six senior registrars in surgery should spend two years of their appointments at St. Mary's Hospital and two years in regional hospitals. The following regional hospitals have been asked to take part in the scheme: Paddington Hospital, Ashford Hospital, and West Middlesex Hospital.

Royal College of Obstetricians and Gynæcologists

Prof. Miles H. Phillips is to deliver the William Meredith Fletcher Shaw lecture at 1, Wimpole Street, London, W.1, at 2.45 P.M. on Friday, Sept. 26. He will speak on Percivall Willughby's Observations in Midwifery.

Institute of Laryngology and Otology

On Friday, Sept. 12, at 5 P.M., at the institute, 330, Gray's Inn Road, W.C.1, Dr. Norton Canfield, of Yale University, will open a discussion on the Analysis of Clinical Hearing Records.

Royal Institute of Public Health and Hygiene

On Wednesday, Oct. 15, at 4.30 P.M., Dr. W. D. M. Paton will deliver the Bengue lecture at the institute, 28, Portland Place, London, W.1. He is to speak on the Uses of the Methonium Compounds.

Postgraduate Courses for General Practitioners at Cambridge

During 1952–53 a series of one-day symposia for general practitioners will be held on Saturdays at Addenbrooke's Hospital, Cambridge. Each symposium will consist of three to five lectures or lecture-discussions and demonstrations of clinical cases or modern methods. The following programme has been arranged: nervous diseases (Oct. 25); obstetrics and gynæcology (Nov. 22); surgical diagnosis and minor surgery (Dec. 20); radiotherapy (Jan. 24); dermatology (Feb. 28); orthopædics and fractures (March 28); cardio-vascular diseases (April 25); common fevers (May 30); pædiatrics (June 27); diseases of the ear, nose and throat (July 25); diseases of the eye. Further information may be obtained from the secretary of the Medical School, University of Cambridge.

British Postgraduate Medical Federation

On Tuesday, Oct. 7, at 4.45 P.M., at the Senate House of the University of London, Malet Street, W.C.1, Prof. J. Z. Young, F.R.S., is to give the opening lecture of the 1952–53 course on the Scientific Basis of Medicine. He is to speak on the Influence of Language on Medicine.

King's College Hospital, London

Dr. F. M. R. Walshe, F.R.S., will deliver the opening address of the session at the medical school, Denmark Hill, S.E.5, on Friday, Oct. 3, at 3 P.M. The annual dinner of past and present students will be held at the Savoy Hotel, W.C.2, on Saturday, Oct. 4, at 7.45 P.M.

University College Hospital, London

On Tuesday, Oct. 7, Sir Wilson Jameson will deliver the opening address of the session at the medical school, University Street, W.C.1, at 2.50 P.M. A course of postgraduate demonstrations for old students of the hospital will be given at the hospital on Oct. 30 and 31. Dr. F. M. R. Walshe, F.R.S., will take the chair at the annual dinner, which is being held at the Savoy Hotel at 8 P.M. on Oct. 31.

Barclay Prize

The late Dr. A. E. Barclay bequeathed £1000 to the *British Journal of Radiology*. The council of the journal has decided to use this bequest to offer a Barclay prize. The prize will normally be awarded annually to the author of the best account of original work in diagnostic or experimental radiology.

The first award will be made in 1953, and candidates should inform the editors of the probable title of their essay, with a brief indication of the nature of its contents, not later than Sept. 30, 1952. The closing date for the receipt of essays is Dec. 31, 1952. Further particulars may be had from the editorial secretary, 32, Welbeck Street, London, W.1.

Prescriptions in July

The Ministry of Health announces that in England and Wales during July the number of prescriptions declared to be submitted was 15,326,000, which was a decrease of 5·5% on the total for July, 1951. The number of forms declared to be submitted was 9,127,000 (decrease 11·6%); and the ratio of prescriptions to forms was 1·68 (1·57 in July, 1951). This year prescriptions for July were 909,000 more than in June. In 1951, July prescriptions were less than in June (as is usual); the difference was about 833,000.

Remuneration of General Practitioners

For the quarter ending Sept. 30, 1952, practitioners are to receive remuneration at the same rate as under the old arrangements together with a provisional supplement, proportional to the first amount, from the money made available by the Danckwerts award (E.C.O. 68/52). It is proposed to apply the same method of payment to the quarters ending Dec. 31, 1952, and March 31, 1953. The sum which has been paid into the central pool as a result of the Danckwerts award is at present provisional. It will be finally determined after March 31, 1953, and any necessary adjustments to the amounts already paid to executive councils will be made then.

As an interim measure the drug capitation fee is to be increased from 6*s*. 6*d*. per annum to 9*s*. 9*d*. with effect from April 1, 1952.

Congress on Rheology

The second International Congress on Rheology will be held at Oxford from July 26 to 31, 1953, under the presidency of Sir Geoffrey Taylor, F.R.S. Further particulars may be had from Mr. G. W. Scott Blair, D.SC., the University, Reading.

London College of Osteopathy

A postgraduate course for registered medical practitioners to be held at the college will begin in October. Further particulars may be had from the secretary of the college, 25, Dorset Square, London, N.W.1.

Pakistan Medical Association

Pakistani doctors in this country have formed a United Kingdom branch of this society. The following office-bearers have been elected: president, Dr. S. D. Jouhar; secretary and treasurer, Dr. M. Shaffi (19, Bernard Street, London, W.C.1); committee members, Dr. T. H. Moghul, Dr. A. M. Akram, Dr. K. Y. Ansari, Dr. Saif-ud-Din Ahmad, and Dr. Mohd Abdul Rashid.

International Congress for Microbiology

The sixth International Congress for Microbiology will be held in Rome from Sept. 6 to 12, 1953, under the presidency of Dr. V. Puntoni. Further particulars may be had from the secretariat of the congress, Istituto d'Igiene (G. Sanarelli), Città Universitaria, Rome.

Course on Rehabilitation in Scandinavia

A group-training course on the Rehabilitation of the Adult Disabled is to be held in Sweden, Finland, and Denmark from Sept. 8 to Nov. 8. It has been organised by Dr. Harold Balme under the auspices of the United Nations, the World Health Organisation, and the International Labour Organisation.

Control of Medical Man-power

Mr. A. Lawrence Abel has replaced Mr. J. B. Oldham as a representative of the Royal College of Surgeons on the Central Medical Recruitment Committee for England and Wales; and Sir William Marshall has replaced Mr. Thomas Hunter as a representative of the Scottish Executive Councils' Association on the Scottish Central Medical Recruitment Committee.

Orphans' Pensions and Children's Allowances

In view of the increase in the family allowance rate to 8*s.* a week, the Minister of National Insurance has made regulations (1952 S.I. no. 1559. H.M. Stationery Office. 3*d.*) adjusting benefits for children payable under the old Contributory Pensions Acts. People receiving an orphan's pension or child's allowance and having at least two children in the family should inquire from the local national insurance office whether they are eligible for an increase. The regulations do not affect orphans for whom a guardian's allowance or industrial death benefit is in payment.

Unusual Foods for Human Consumption

The Nutrition Society is holding a conference on this subject at Bedford College, London, N.W.1, on Saturday, Oct. 18, at 10.15 A.M. The following papers are to be read: Seaweeds and their Value in Food-Stuffs (W. A. P. Black); Mushrooms and Toadstools (J. Ramsbottom); Insects as Food (W. S. Bristowe); Indigenous Foods of Central America (F. Aylward); Diet of Canadian Indians and Esquimeaux (H. M. Sinclair); Food of Australian Aborigines (G. H. Bourne); Protein in the Diet of the Isoko tribe of the Niger Delta (B. M. Nicol). Further particulars may be had from the programmes secretary, Mr. R. J. L. Allen, Monkhouse & Glasscock Ltd., Snowsfields, London, S.E.1.

Present Problems in Nutrition Research

The International Union of Nutrition Sciences is holding a symposium on this subject at Basle from Oct. 1 to 4. The speakers will include: Dr. J. Trémolières (Paris), Prof. A. I. Virtanen (Helsinki), Dr. D. P. Cuthbertson (Aberdeen), Prof. E. Crasemann (Zürich), Prof. E. J. Bigwood (Brussels), Prof. K. Lang (Mainz), Prof. K. Bernhard (Basle), Prof. K. Thomas (Göttingen), Prof. O. Högl (Berne), Prof. E. Abramson (Tomteboda, Sweden), Mr. S. J. Folley, D SC., F.R.S. (Reading), Prof. A. B. L. Beznák (Birmingham), Mr. L. J. Harris, D.SC. (Cambridge), Prof. H. Dam (Copenhagen), Prof. H. D. Cremer (Mainz), Prof. V. Demole (Lausanne), Dr. W. R. Aykroyd (F.A.O., Rome), Prof. A. C. van Veen (F.A.O., Rome). Further information may be had from the secretariat, c/o *Experientia*, Verlag Birkhäuser A.G., Basle, Elisabethenstrasse, 15, Switzerland.

Medical Mycologists

The committee on medical and veterinary mycopathology of the International Association of Microbiologists has compiled an international address list of medical mycologists. Copies (1*s.*) may be had from the Commonwealth Mycological Institute, Kew, Surrey.

No. 2 (Br.) General Hospital

The sixth reunion dinner of this hospital will be held at Simpson's Restaurant, Strand, London, W.C.2, on Saturday, Oct. 4. Tickets may be had from Dr. J. H. Easton, 25, Biddenham Turn, Bedford.

Graduated Beakers for Injectable Fluids

A new British Standard has been published (B.S. 1847:1952) for graduated beakers for injectable fluids (for hospital use). This specifies graduated heat-resistant glass beakers of 50 ml., 100 ml., and 300 ml. capacity. Copies of the standard (price 2*s.*) may be obtained from the British Standards Institution, Sales Branch, 24, Victoria Street, London, S.W.1.

King Edward's Hospital Fund are now issuing a second edition of their series of catering circulars. The following are available: Use of the Meat Ration, Care of Catering Equipment, Layout and Design, Sources of Waste in Catering, and Rations and Rationing. The circulars are issued free to hospitals, and copies can also be obtained (1*s.* post free) from the offices of the Fund, 10, Old Jewry, London, E.C.2.

During September Dr. Earl R. Loew, professor of physiology in Boston University School of Medicine, is acting as guest professor in the department of pharmacology and therapeutics, St. Andrews University Medical School, Dundee.

Prof. Robert Cruickshank, Dr. Thomas Anderson, and Dr. W. C. Cockburn are visiting Yugoslavia during September, under the ægis of the World Health Organisation, to conduct refresher courses in the control of communicable diseases at the main medical centres there.

The headquarters of the Ministry of National Insurance are now at 10, John Adam Street, London, W.C.2 (Telephone: Whitehall 9066).

Appointments

BARBER, J. M., M.D. Belf., M.R.C.P.: consultant physician, Ards Hospital, Newtownards and Bangor Hospital, Bangor.

BATES, J. L., M.B. Lond., M.R.C.P., D.P.M., D.C.H.: asst. psychiatrist (S.H.M.O.), Borocourt Institute for Mental Defectives, near Reading.

BULSTRODE, J. C., M.R.C.S., D.M.R.: consultant radiologist, Princess Elizabeth Hospital, Guernsey.

DE FONSEKA, C. P., M.B. Ceylon, F.R.C.S.: surgical registrar, Bath group of hospitals.

EDGCUMBE, J. O. P., M.A., M.D. Camb.: consultant pathologist, Exeter clinical area.

EDWARDS, C. H., M.R.C.P.: clinical asst. (part-time), department for nervous diseases, St. Mary's Hospital, London.

FITZMAURICE, W. J., M.B. Birm.: appointed factory doctor, Alcester district, Warwickshire.

GUILD, Euphemia, M.B. Edin., D.P.H.: asst. school M.O., Huddersfield.

JONES, H. M., M.B. Lond., F.R.C.S., D.L.O.: part-time consultant in otolaryngology, Royal Eye and Ear Hospital, Bradford.

MAITLAND, D. R., M.B. Edin., F.R.C.P.E., D.D.R.: consultant radiologist, radiological department, Royal Infirmary, Edinburgh.

MULHALL, P., M.B. Dubl.: asst. chest physician, Brecon and Radnorshire area, with clinical duties at Highland Moors Sanatorium and the Adelina Patti Hospital, near Swansea.

SINCLAIR, W. W., M.B. Glasg., D.P.H.: senior M.O. (schools), Fife.

STEWART, I. S., M.D. Leeds: consultant in pathology, hospitals in the Bingley, Keighley, Skipton and Settle group, with duties at the Hospital, Middleton-in-Wharfedale, and the Hospital, Grassington.

ZALESKI, WITOLD, M.B. Polish School of Medicine, Edin.: asst. psychiatrist (S.H.M.O.), Pewsey Hospital for Mental Defectives.

University College Hospital, London:

GREAVES, D. R., M.B. Sheff., F.R.C.S., D.O.M.S.: consultant ophthalmic surgeon.

KINGDOM, L. G., M.B. Camb., F.R.C.S.: consultant E.N.T. surgeon.

POND, D. A., M.D. Camb., M.R.C.P., D.P.M.: consultant physician, department of psychological medicine.

East Anglian Regional Hospital Board:

JUBY, H. B., M.B. Lond, D.L.O.: E.N.T. registrar, Norfolk and Norwich Hospital.

SUTTON, P. H., M.D., B.SC. Lond., M.R.C.P.: consultant chest physician, Norwich area chest clinic.

WORKMAN, J. M., B.M. Oxfd: senior registrar in chest medicine, Ipswich area chest clinic.

The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

PROGRESS IN THE TREATMENT OF BREAST CANCER*

D. W. SMITHERS
M.D. Camb., F.R.C.P., D.M.R.
PROFESSOR OF RADIOTHERAPY IN THE UNIVERSITY OF LONDON AT THE ROYAL CANCER HOSPITAL

I HAVE chosen the subject of Progress in the Treatment of Breast Cancer for several reasons, chiefly because it was this disease which prompted the foundation of this lecture, but also because it provides a good illustration of the theme, within the general title laid down, which I think most requires discussion at the present time. This theme is the need for a return from the "universal cause and cure" attitude, which has inspired so much experimental cancer research and has widely infected the medical profession, to the clinical view of the human problem which it really is. We are in danger of becoming bemused by a wealth of disconnected and impressive scientific detail into believing that the research-worker is nearer to the problem than the doctor, when the reverse is the case.

The clinical view, however, needs to be revitalised so that advancement in knowledge may find a practical expression helpful in prevention and treatment. The oversimplified clinical view which has so long been the basis of our treatment methods has led us into a far too rigid and largely false division of cancer patients into those in whom we must make as rapid and as drastic an attempt at cure as possible, and those whom, because we regard the situation as hopeless, we abandon either to a half-hearted attempt at palliation or to the quacks who provide the encouragement we fail to give.

On Progress

Halsted looking back in 1897 concluded that up to that time no woman with breast cancer had ever been cured. There are those today who think that not only was he right then but that there has been little fundamental change in the situation since his time. They wave aside our survival-rates, the evidence which their predecessors in scepticism had demanded from us, point to our failure to make a drastic reduction in the general breast-cancer death-rate, assure us that there are no grounds for our fond belief that the earlier we give our treatment the greater the chance of cure, and assert that those patients whom we so carefully pick out to treat would live as long if we did nothing. These people are not clinicians, not theirs the daily decision of what to do for Mrs. Jones who has arrived with a frightened husband, an anxious daughter, and a lump in the breast. They are pathologists, hygienists, biometricians, and statisticians, the pyrrhonists of medicine whose facts are not regularly warmed by compassion. It is most important that we listen because we may learn. They will at least keep us from complacency, though those of us who regularly deal with cancer patients are not lightly to be accused of this failing. We may, however, comfort ourselves with the assurance that their figures do not contain the whole of truth and that they are in some danger of coming to know the significance of everything and the value of nothing.

If we are to allow ourselves to speak of progress we must take a realistic view of the past, examine the basis for our present beliefs and practice, and plan the future so as to promote the best interests of our patients and not those of surgery, radiotherapy, chemotherapy, or even the Registrar-General's annual report.

RELIEF OF SUFFERING

In looking back over the past for signs of progress I would put first relief of suffering. This is not something we can arrange on a table or fit into a chart. Surgery removes the anxiety of the presence of a lump in the breast, and, as judgment has improved, has continued to prevent the discomfort of ulceration while steadily reducing the incidence of local recurrence. We cannot compute a figure to express the value of hope supplied or of relief from the worry, pain, and distress which would have gone with the steady local advance of a tumour. We cannot put these benefits into a survival-rate for patients who develop distant metastases and live no longer than they would have done untreated. Surgery, looking back over the years, has solid cause to congratulate itself on the relief of suffering it has achieved for patients with breast cancer.

Radiotherapy in its comparatively short life has already established a claim to be considered the most valuable means of palliation at our disposal for patients with malignant disease. It assays one of the most difficult tasks in medicine. It is confronted daily by human tragedy which makes incessant demands for cheerful reassurance or gradual enlightenment—demands that tax our humanity, understanding, and ingenuity to the full. It requires an acquaintance with a wide field of clinical medicine and the ability to work closely, harmoniously, and often most unselfishly, with many different surgeons. The safety of the patients and of the workers in these departments, as well as the efficient conduct of treatment, cannot be assured without a high degree of technical proficiency in a complicated branch of applied science. The degree of progress in the relief of suffering of patients with breast cancer for which it has been responsible can be appreciated at once if we consider how we should now get along without it in those hospitals where hundreds of these patients present themselves for our help each year.

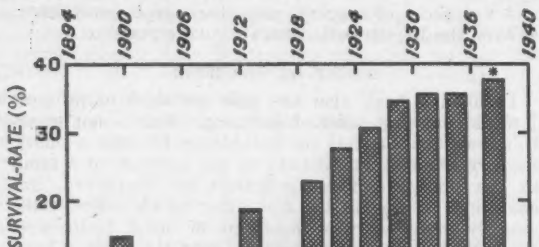
Surgical castration was used before X rays were discovered; ovarian irradiation has been employed for thirty years; and hormone treatment has for the past fourteen years come to join surgery and radiotherapy in the treatment of breast cancer patients. After all this time we are still uncertain about their future possibilities. We can, however, see relief obtained quite dramatically at times which was not obtainable before, and is still not obtainable by any other means. Great interest is aroused by the chance to influence disseminated tumours either directly or by alterations in the environment in which they grow. The possibility of learning more about the control of growth and of adding to the efficiency of our tumour treatment methods that hormone therapy has provided is a spur and a challenge.

All this I regard as good evidence of progress.

LONGER SURVIVAL

I have taken relief of suffering first because it seems to me to be one of the chief duties of medicine; but we like to think that we save life and persist in judging our efforts by the sometimes dubious criterion of survival. The only continuous record of survival of all new patients with breast cancer attending one hospital since the introduction of serious attempts at treatment that I know of is that of the Massachusetts General Hospital (Taylor 1949). This remarkable record is almost complete from 1894 to 1940 (fig. 1). If we place these results in a time relationship with those obtained in other hospitals where all new patients seen, whether treated or not, have been included, we can see that it is a fair representation of the state of affairs in such centres

* The First Dorothy Platt memorial lecture, given at King's College Hospital Medical School on July 1, 1952. This lecture was established by the late Mr. J. B. Hunter, to whom Miss Dorothy Platt gave a donation to be used for the advancement of the knowledge of cancer.



*The figure of 38% for 1936–40 is based on the assumption of an operability-rate of 75% for those years, it having varied from 71% to 80% during the preceding 40 years and the total new cases seen for 1936–40 not being in the text.

Fig. 1—Results of treatment in patients with cancer of the breast attending the Massachusetts General Hospital from 1894 to 1940, calculated from the "total primary cases."

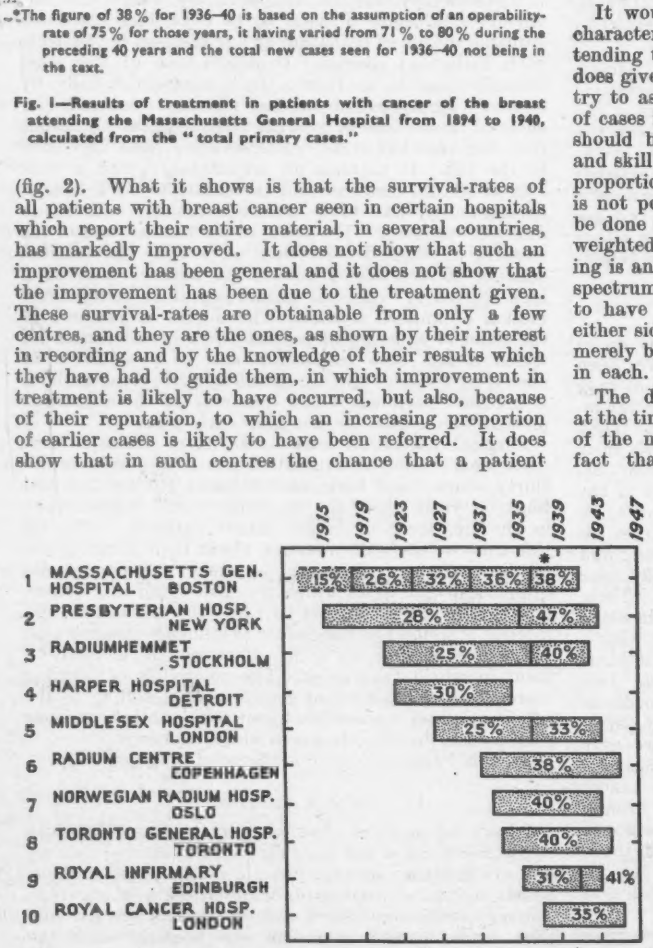
(fig. 2). What it shows is that the survival-rates of all patients with breast cancer seen in certain hospitals which report their entire material, in several countries, has markedly improved. It does not show that such an improvement has been general and it does not show that the improvement has been due to the treatment given. These survival-rates are obtainable from only a few centres, and they are the ones, as shown by their interest in recording and by the knowledge of their results which they have had to guide them, in which improvement in treatment is likely to have occurred, but also, because of their reputation, to which an increasing proportion of earlier cases is likely to have been referred. It does show that in such centres the chance that a patient attending with breast cancer will survive five years has probably been more than doubled in the last thirty years.

This improvement could be due to a number of things. It could be due to a change in the selection of patients attending the hospitals which record their results; it could be due to a change in the type of tumours developing, with a swing towards a less malignant character; it could be due to an improvement in speed of diagnosis and in time of starting treatment; it could be due to an improvement in diagnosis resulting in the inclusion of more less-malignant tumours in the total recorded by adding some which had previously either been missed or regarded as non-malignant; it could be due either to improvement in the methods of treatment themselves or to a better selection of treatment method for each individual patient; lastly, it could be due to some combination of these factors.

Change in Malignancy of Tumours

It would be difficult to prove or disprove that the character of breast cancer has changed with the years, tending to become less malignant. Histological grading does give an indication of malignancy, but if we were to try to assess such a trend by comparing the proportion of cases in each histological grade from time to time we should be confused by differences in grading methods and skill and, even more important, by differences in the proportions of tumours graded. Since accurate grading is not possible with small pieces of tumour it can only be done on operable patients whose tumours are heavily weighted towards the more differentiated. Since grading is an arbitrary division into sections of a continuous spectrum of degree of differentiation, usually arranged to have a large central group with smaller groups on either side, it is not easy to observe any gradual change merely by listing from time to time the proportion found in each.

The degree of clinical advancement of the disease at the time the patients are first seen is in part a reflection of the malignancy of the tumours concerned, and the fact that the operability-rate at the Massachusetts General Hospital has not changed in fifty years suggests that there has been no marked trend towards a diminution in malignancy. An improvement in stage distribution has occurred, however, in some other centres, notably Radiumhemmet, corresponding with their improvement in results, and it is debatable how far such trends may be due to earlier diagnosis, better selection, or alteration in character of the tumours. There does not seem to be any real evidence on which we would be justified at present in making the assumption that the character of breast cancer is changing.



*On the assumption that the operability-rate has not changed and that the total number of new patients seen during this period was 527.

Fig. 2—Variation of absolute survival-rate with date of treatment in patients with cancer of the breast.

(1) Taylor 1949. (2) Haagensen and Stout 1942, Haagensen 1949. (3) Berven 1949, Nohrman 1949. (4) Evans and Leucutia 1939. (5) Truscott 1947, Windeyer 1949. (6) Kaae and Nielsen 1951. (7) Engelstad 1948. (8) Richards 1948. (9) McWhirter 1948, 1949. (10) Smithers et al. 1952.

Improved Diagnosis

Improved diagnosis may have resulted in the inclusion of some patients omitted altogether in the past, or some tumours previously regarded as non-malignant. If so, there may have been a change, not in the nature of the disease, but in the selection of an increased proportion of more favourable cases in the groups reported. Certain benign lesions of the breast may simulate cancer—e.g., adenosis, fat necrosis, tuberculous mastitis, the badly named granular cell "myoblastoma," and plasma-cell mastitis—and some circumscribed carcinomas may be mistaken for benign tumours or cysts. On balance improved diagnosis should tend to detect and so reject

more non-malignant tumours which might have been included in the past, than discover and so include malignant tumours which might have been omitted.

An important influence here might be a real change of opinion about a group of tumours formerly regarded as benign and now thought of as malignant. I know of no such general swing of opinion in breast cancer, though there are considerable differences in interpretation between pathologists, particularly with regard to the dividing line between duct papillomas and duct carcinomas. There does not seem to be good evidence that improved methods of diagnosis have increased the proportion of the less malignant tumours in the patients recorded as having breast cancer though it would be difficult to show that this were not so.

Reduction of Delay in Starting Treatment

Those who are most persistent in telling us that there is no evidence of improvement in survival due to treatment also maintain that early diagnosis makes no difference to the prognosis. This is not so. Prognosis probably depends more on the type of tumour that a patient develops than on any other factor since this so largely determines the degree of advancement of the disease by the time the patient starts treatment (see table). Patients with slow growing breast tumours may present themselves at hospitals for the first time having noticed a lump for many months and still survive for many years after treatment. A group of patients with long histories will in fact contain a high proportion with the less malignant tumours, since if they had developed more malignant ones at the same time and had had no treatment they would have been dead. With the more malignant tumours early treatment is of great importance. Many will have metastasised before the patient is first seen but the sharp deterioration which occurs in survival time with histories of three months or more is an indication of the importance of speed in this group.

Unfortunately there is not much real evidence of any decline in the period of delay which occurs between noticing the first symptom and starting treatment. Figures giving the change in average delay do not give a clear picture of the important issue, since it is only during the first two or possibly three months that delay is of much importance. Quite a few patients with a good prognosis and histories of two, three, or more years may well produce a misleadingly high figure for the average delay.

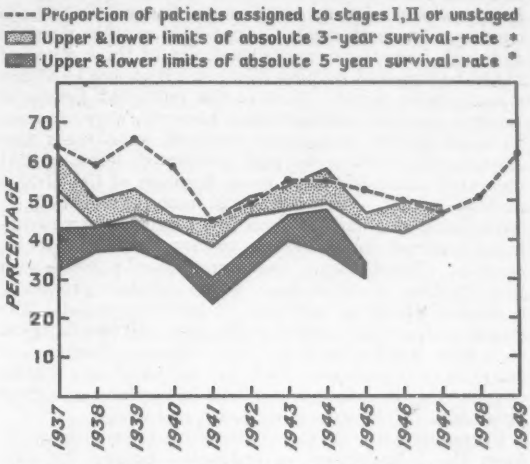
Changes in Selection of Patients

The selection of patients attending the hospitals where complete records are kept and where results are published may well account for the differences in survival-rates between them. To see if it may not have accounted for the improvement in results over the years within any one hospital we need evidence that this improvement has not merely followed a change in stage distribution. We have just seen that there has been no change in operability-rate at the Massachusetts General Hospital in fifty years. At other centres the position is different; at Radiumhemmet for instance the proportion of early cases increased from 50% to over 70% for the periods 1921–35 and 1936–41. In my own hospital there has been no steady change in the stage distribution, but since 1937 there have been fluctuations from year to year. A decline in the percentage of early cases during the first war years was clearly reflected in a corresponding fall in survival-rate (fig. 3). Definitions of staging and of operability are sadly lacking in uniformity, and comparisons are most difficult. It is clear, however, that the results obtained are closely dependent on the material treated and that alteration in this alone may well account for much of the change in survival-rate which, when it moves in the right direction, we attribute to our therapeutic skill.

SURVIVAL OF PATIENTS WITH OPERABLE BREAST CANCER ACCORDING TO AXILLARY LYMPH-NODE INVOLVEMENT AND GRADE OF MALIGNANCY OF TUMOUR

(Based on 482 patients seen at the Royal Cancer Hospital, 1937–1950 for whom the necessary details were recorded. Graded by Dr. M. Thangavelu.)

Grade	Lymph-nodes not involved		Lymph-nodes involved		Proportion of patients with lymph-nodes involved
	(No. of patients)	% surviving: 5 years / 10 years	(No. of patients)	% surviving: 5 years / 10 years	
I	(45) ..	90·6 / 68·0	(37) ..	77·8 / 29·5	45%
II	(96) ..	74·4 / 57·6	(224) ..	34·0 / 14·9	70%
III	(12) ..	28·2 / 28·2	(68) ..	6·2 / 0·0	85%



*According to whether untraced patients are regarded as alive or dead.

Fig. 3—Results of treatment of patients with cancer of the breast at the Royal Cancer Hospital set in relation to variation in proportion of patients in early stages.

A DOWNWARD TREND

There are a number of reasons why there has been no great fall in the general mortality-rate from breast cancer. It is not in itself an argument against treatment having improved in the better centres, since they deal with only a small proportion of the total and since no more than a gradual and limited improvement can be expected with existing methods. There are also difficulties with death certification since the tendency to record death as due to breast cancer in any patient who has once had the disease is so strong. Until 1940 in fact, the Registrar-General's office often changed the recorded cause of death to cancer when this was mentioned as a subsidiary cause by a doctor who had himself attributed the death to something else. It is going to be difficult to judge the effect of treatment by changes in mortality-rates if we are never going to let a patient who has once had breast cancer die of anything else. With all these difficulties, however, if a correction is made both for the growth of the population and its increasingly adverse age composition a slight downward trend in mortality-rate for England and Wales appears.

Survival without Treatment

Accurate data on the duration of life in patients with untreated breast cancer would be most valuable. The published work agrees in suggesting that the average time from first symptom to death is about three years.

Most treatment results are given in survival-times from treatment to death so that about eight months must be deducted from the suggested average of three years of life to be expected without treatment if we are to obtain a comparable figure. Most of the published figures of survival-times for the untreated, however, were obtained on small groups of patients observed some years ago. Greenwood's well-known and oft-quoted series of 651 untreated patients with a mean duration of life of 38·3 months, a 50% death-rate at 26 months and 75% at 46 months, was derived from five sources, the patients being observed during the first twenty years or so of this century. These contain a small number of patients with long histories, some of many years' duration producing a marked effect on the average survival period. The largest of these groups was taken from my own hospital at a time when elderly patients with long histories of lumps in the breast were often left untreated as a matter of policy because they had a long history and so a good prognosis—not because they had a bad one.

Untreated patients in most hospitals today, especially since the introduction of œstrogen therapy for this elderly group, are few and are usually either those who refuse treatment or those who are thought to be near to death. No idea of the expectation of life in a representative group of patients without treatment could be obtained from such a selected few. It is unlikely that the commonly quoted figure of three years fairly represents the average duration of life from the time they first reach hospital which all patients with breast cancer would "enjoy" if none of them were to be treated, as it is sometimes made out to do; but it may not be so very far out as a representation of the average time that patients who notice lumps in the breast which are thought to be malignant will survive from the moment they first notice them, if we include all those who claim to have noticed a lump for several years and accept this as evidence that they have had a malignant tumour throughout that period.

Successful Treatment

Let us attend carefully to our critics, by all means; let us examine the basis for our belief that treatment prolongs life as well as relieves suffering; but let us hold on to common sense. It is asking a lot to expect us to accept the view that so long as a patient has been treated in the early stages of the disease we may never regard our treatment as successful while she lives (nor even if she dies from some other cause unless a detailed post-mortem examination has been made) but that we must acknowledge failure whenever a patient dies from the disease, dies with the disease still present, or even dies without clinical signs of the disease if recorded as a cancer death by the doctor, however long the interval from treatment, or the period of freedom from symptoms may have been, and whatever degree of relief of suffering may have been achieved.

On Belief

My generation has not suffered (if that is the right word) from a belief in the inevitability of progress. The old confidence in the future has had too much to contend with in our time. We were young in an age when writers were making the discovery "that the world is not wholly charming, that life is brutal, tiresome and vulgar, and that no decent person should have been invited to so squalid a party." We were not so disillusioned because we had not known the "good old days," but we could hardly adopt a happy optimism except through faith. We were taught that man's desire for certainty was an intellectual vice and that all our knowledge was more or less vague, but we also came to appreciate in a hard school the need for firm action if anything was to be achieved. To be resolute without belief, to act on the best hypothesis available while accepting its imperfections and preparing to abandon it when a better one appears, does not come so easily. It is humour that makes it possible by easing us gently from those of our beliefs, entrenched by prejudice and self-interest, which we find it most painful to doubt.

We realise that progress in the treatment of patients with breast cancer depends upon our accepting uncertainty, prodding ourselves out of the beliefs that what we know how to do must be the best for our patients, and that any improvement that may have occurred must have been due to our own personal efforts, and then firmly carrying into action a working hypothesis some of the imperfections of which are quite clear to us.

UNDERLYING ASSUMPTIONS

The conception of breast cancer on which we base our treatment has, I think, changed little in fifty years; it rests on the assumption that a sudden specific change takes place, for some reason unknown, in a cell in a woman's breast so that it acquires autonomy and begins to grow relentlessly and uncontrolled, by direct extension to start with but soon by embolism as well, first to the axilla and later elsewhere, until its local extent or distant dissemination render life impossible. From this follows the beliefs that the only hope of cure lies in the immediate removal of sufficient tissue to include the whole limit of spread that has so far taken place, that the earlier and more drastic the operation the greater the chance of cure, and that radiotherapy, while useful as a means of growth restraint and for relief of symptoms, can have little real effect upon the course of the disease. Reliance on radical mastectomy as the one real hope in treatment for so many years even in quite advanced cases has been based on just such simple concepts. They have had the merit of providing a good working hypothesis which could be firmly pursued; but knowledge has advanced and we must ask if we have clung to these simple views too long.

There are always those who are not prepared to question their old beliefs or doubt the value of a procedure at which they have themselves acquired much skill. With regard to breast cancer the ground under them has been rudely shaken by developing concepts of the complicated nature of malignant disease of the breast in man and other animals, by the curious effects that may be produced in women with breast cancer during pregnancy or at the menopause, by the irregular changes that result from time to time when hormones are administered, by an act of filial piety at the Middlesex Hospital, by a quiet, persistent voice from Edinburgh, backed by a fine array of facts, and by the steady development of radiotherapy. The idea of a single focus of malignant growth is giving way before the theory of a field of origin, the multiplicity of breast tumours and the frequency of bilateral disease has to be accounted for. The belief in a sudden change must be considered in the light of the evidence for a continuous gradation in several different aspects of both structure and behaviour from the most benign to the most malignant characteristics. The complete autonomy of the tumour cell is hard to credit in the face of spontaneous regression at the menopause, acceleration of growth at pregnancy, response to hormone treatment, or even the frequency and distribution of metastases, surely untenable on a purely mechanical basis.

We need an explanation of how a tumour focus may lie dormant for thirty years in a mastectomy scar only to start to grow again at the time of the appearance of a new primary tumour in the opposite breast. We must ask why, with more advanced disease, the results of more radical surgery become worse not better than those of less radical surgery. We must wonder how we managed to rely so much and for so long on radical

mastectomy if Richard Handley (1952) can now show that 75% of patients with inner-half tumours, and 30% of those with outer-half tumours, who also had axillary-node involvement, already had parasternal nodes involved as well, while a few others had parasternal-node involvement without any invasion of the axilla. We cannot ignore McWhirter's Edinburgh experiment (1948, 1950) which has produced survival-rates as good as any and better than most without employing radical mastectomy at all.

Animal work has recently confirmed—and so, in our curious scientific world, made respectable—long-standing clinical observation of the fact that what we call "malignancy" in a tumour is not a single indivisible character but a type of behaviour resulting from the interplay of a number of properties and manif sted in a certain environment. The irregular distribution of metastases displaying the favourable conditions for growth in the suprarenals as compared with the spleen, for example, is well known. Tumours change; they progress in growth-rate, in invasiveness, in tendency to dissemination; they vary from time to time and place to place in responsiveness to external stimuli and in the surrounding tissue reponse which they provoke. Tumours with disproportionate characteristics are familiar to us all: those which invade but do not metastasise, those which metastasise but without much local invasion; the small early tumour progressing relentlessly and the massive established growth which still responds well to treatment. The variation in behaviour and responsiveness between metastases in a single patient has been brought out even more clearly since hormone treatment was introduced. Foulds (1951) has suggested that responsiveness to external stimuli in breast tumours may be similar to the state known as "conditional tumours" in animals where the tumour persists only so long as the carcinogenic stimulus is applied. Progression to a non-responsive state may occur, or some new and usually less carcinogenic stimulus may at times cause the reappearance and progression of a conditional tumour. The position is not so simple as our old beliefs suggested; several factors are involved in the behaviour of tumours, each one of which may appear and change independently of the others. Our attempts at definitions of cancer have usually involved a list of such characters on the assumption that they were either present or absent, now we have to consider what degree of each we shall demand for our definition and will have to admit that there is no sharp dividing line between benign and malignant tumours—only a variation in a pattern of behaviour.

RADICAL MASTECTOMY

Faced with considerations such as these, how are we to adapt our treatment policy to the new conceptions? Are we to wait for the "cancer cure?" Even if we are the sort of people who prefer to sit down quietly and believe in a panacea, we should not as we wait decry the efforts of those who continue energetically to develop the lines of treatment which have already proved effective.

Radical mastectomy was by design for the few. It had its greatest volume of "success" when there was no evidence of the axillary involvement for which it was performed, but its greatest achievement was in those few patients—and we are learning how few they were—in whom the disease had spread to the axillary nodes but to nowhere else. Its misfortune has been that it became the treatment for the many. It would be a disaster if we were either to discard it lightly or to regard it forever as the last word in breast-cancer treatment. Its unique position is now giving way. On the one hand it is yielding before the surgical enthusiasts who do not willingly entertain the idea that they may ever spread the disease, remain certain that what they can do well must be for the best, are not much concerned with metastases since they are solely bent on cure of local disease, but who, having been surprised into finding that their local treatment has often been inadequate, meet the situation by still more radical procedures—despite the fact that some 20% of patients with no axillary lymph-node involvement and some 50% of those with nodes involved already have distant metastases at the time of operation. On the other hand it is going down before the more conservative surgeons, some persuaded by their radiotherapy colleagues, who have more truly appreciated the situation but who have reacted by giving up any attempt to clear the axilla instead of by trying to define more accurately the indications for this proved and valuable procedure. These very different outlooks have the merit of simplicity; they each provide an understandable and practical working hypothesis which can be firmly pursued. We shall learn much from both of them, but they have the defect of being applications of simple uniform plans to a varied and complicated problem. We should with thought be able to do a little better.

RADIOTHERAPY

It is not only our view of the rôle of surgery which has suffered from over-simplification. Radiotherapists, with less reason, have concentrated just as much on the direct destruction of every tumour cell as the only hope of cure. Their belief in their ability to bring about the immediate death of all tumour cells by doses within the therapeutic range has been in direct opposition to the evidence and has led to neglect of important stromal and tumour-bed reactions. Their attachment to "tumour-lethal doses," sometimes without any allowance for volume treated or amount of normal tissue included, and their talk of "therapeutic ratios" as though these were simple relationships between "tumour-lethal doses" and "normal tissue tolerances" are but examples of the crude and caustic rôle they have themselves so often assigned to their refined and much-abused method of supplying energy to the tissues.

Tumour cells grow by virtue of a breakdown in the normal coördinating mechanisms of the body and by courtesy of the stroma and tumour bed by which the body provides for their needs. The environment cannot be divorced from the cell in considerations of disorders of growth any more than it can in considerations of normal growth; there is much tumour embolism without the formation of metastases. When radiotherapy acknowledges its debt to the normal tissue reactions it does so little to preserve, and attempts to combine its inhibiting effect on tumour cells with the promotion of the normal mechanisms by which the body achieves coördination, it may develop further from an empirical method of near-cauterisation into a delicate scientific means of altering tissue relationships. It may then be employed as part of an integrated treatment scheme in which, acting as the selective local depressant factor, it may more frequently allow the normal tissue reactions to assert themselves and re-establish the dynamic equilibrium of coördinated growth and repair.

On Practice

While it is easy to confuse the picture by a recital of complicated experimental or detailed clinical observations, it is not so simple to find a new working hypothesis to replace the old. The first step in deciding on treatment practice is to be quite certain what we want to achieve. We know that we can prevent some forms of cancer, or at least so long postpone their development that it amounts to the same thing since the patients die of something else. (They must still die. Life has a 100% mortality and death is a necessity for evolution.)

We know that we can remove the disorganised tissue in some of the less active and more localised growth disorders so that the patient lives his normal span of life without recurrence, but we also know that he may harbour a tumour focus for twenty or thirty years without knowing it, only for it to wake to activity at last to cause his death. The wonder is not that disorganisation of the normal processes of growth and repair occur, or that their manifestations are so varied, but that we maintain so long as we do our wonderful steady state despite our extraordinary internal turmoil. We had to wait for radioactive isotopes to tell us just how extraordinary that ordered turmoil is.

The wide variety of degree of incoördination of growth which we cover by the vague word cancer is one of the universal ways in which living things decay and die. As accidents and infections are warded off and life is prolonged, death depends more and more on the degenerative diseases for its necessary toll. The more we understand about the particular relaxations, stresses, strains, and irritations which chiefly predispose to the disorganisation of growth control in various tissues, the better shall we be able to postpone the day when restraint breaks down. The more we learn about the earliest manifestations of such disorganisations, the more quickly shall we be able to deal with the situation before it has got out of hand. The more we know of the natural history of growth disorders at different sites and can assess the degree of disorder and extent of spread reached, the more efficiently shall we be able to choose and apply our treatment methods.

PRESCRIBING TREATMENT

In a general discussion of this kind a detailed account of a treatment plan for patients with cancer of the breast would be out of place. Such an account needs setting in a framework of general principles, the reasons for accepting which are given, together with the evidence on which each one is based. These principles must be interpreted in the light of the needs of each individual patient. Patients vary as much in personality and circumstances as they do in the type of tumour and degree of advancement of the disease with which they present themselves. There is as much difference from one to another in the confidence with which we can rely upon our clinical assessment of the extent of the disease as in the reliance we can place on the history that they give. These things may have an important bearing on the treatment we prescribe. I propose merely to make a few short statements here as illustrations of the kind which I think should colour our view of this treatment problem. They seem to me at the present time to fit in well with the evidence available and to provide a guide to help us make the best use of all the proved treatment methods available. Since several hospitals employing only one or other of these methods as their main treatment plan produce survival-rates of the same order, when allowance is made for differences in material treated, we must either conclude that all these methods have some merit, chiefly exercised in different groups, or that the treatment method used makes little difference to survival, which we know to be untrue for the later cases and which we have good reason to believe to be untrue for the earlier cases also. Patients in the same clinical stage of advancement may still be clearly distinguishable as having a different prognosis and in needing different treatment plans. Radical mastectomy (with postoperative irradiation where indicated), local mastectomy with irradiation of the regional lymph-node regions, and radiotherapy alone or preoperatively, may all have their place within one clinical stage.

The few short statements about the treatment of patients with breast cancer which I would put forward at present to illustrate an approach to the problem are as follows:

1. The outcome of any treatment for patients with breast cancer depends more on the degree of advancement of the disease, which is largely dependent on the nature of the tumours they develop, than on any other factor.
2. Only surgery, radiotherapy, and occasionally hormones have been shown to modify the course of the disease.
3. Surgery is generally more effective than radiotherapy in eradicating breast cancer, both in the primary site and in the axilla; but unsuccessful surgery usually makes matters worse, whereas radiotherapy normally provides at least some degree of improvement and may lead to complete clinical tumour regression lasting many years.
4. The first consideration in treatment is what chance there is that surgery will be successful. When the chance of complete removal of the tumour by surgery does not seem to be good, or the assessment of that chance is difficult, radiotherapy is to be preferred. The breast and the axilla should be considered separately in making this decision. In some of the doubtful cases operation is best performed after radiotherapy.
5. A worth-while estimate of the nature of the tumour, on which the chance of success with treatment so much depends, can usually be made by considering the length of history, good sense of the patient, size of the tumour, and clinical evidence of spread in relation to the ease of making the examination.
6. A sensible patient with a small hard tumour in the outer half of the breast which has been noticed for some months, who is reasonably thin and easy to feel, and has no more than one or two hard mobile nodes low down on the medial wall of the axilla (stage II), is usually best treated by radical mastectomy. Postoperative irradiation should be reserved for those patients in whom detailed pathological examination of the specimen removed suggests that local recurrence is likely, and that the clinical judgment was at fault.
7. A patient with a small hard mobile primary tumour who is either too fat for adequate palpation of the axilla, or who on palpation has several small nodes extending high up into the apex (stage II), is usually best treated by local mastectomy and radiotherapy to the lymph-node regions, especially if the history is short.
8. A patient with a short history and a large tumour in the inner half of the breast with several hard nodes palpable in the axilla (stage II) has a bad prognosis, may never be suitable for operation, and is usually best treated by radiotherapy alone.
9. The more differentiated, slow growing, and localised the tumour, the more reason for primary surgical treatment. The more undifferentiated, rapidly growing, and disseminating, the more reason for primary radiotherapy. In the middle group, when in doubt, it is wise to use radiotherapy first with a view to using surgery later; but if the condition is still doubtful after irradiation, surgery is still to be avoided and reliance placed on radiotherapy and hormones.
10. Careful management and energetic treatment of patients with more advanced disease, avoiding surgery in regions where it is likely that all the abnormal tissue cannot be removed, is often well worth while.
11. In elderly patients with slowly progressive ulcerating breast tumours, œstrogen therapy may be completely successful—i.e., enable them to live their normal span of life without discomfort. Premenopausal women with metastases may be helped, sometimes dramatically, by surgical or X-ray castration. Androgens may sometimes be of value when the castration effect has worn off, or for debilitated patients of any age with widespread deposits especially in bone. In general,

hormone response is infrequent and uncertain and the treatment is at present best reserved for patients with symptoms due to multiple metastases no longer controlled by irradiation. Its combination with X-ray therapy holds out a real prospect of improvement in results as we learn more about their joint action on both the tumour cells and their environment.

12. The most successful palliative treatment may take as much time and care as that designed with a more ambitious aim. At the mere mention of the word palliation the extremes of either giving some easy, quick, ineffectual treatment and then sending the patient home to die under someone else's care, or of pushing treatment till it adds to the patient's discomfort while merely prolonging the act of dying, are still far too often adopted.

Envoy

We can now at times eradicate, we can often delay progress, and usually we can relieve suffering for a time at least; but it seems that more is expected of us not only in the quality of the work we do, which is reasonable, but in its very purpose. The purpose of medicine is surely not to change the whole face of Nature. It is good to set ambition high but not to let our thoughts get out of hand.

> "Couldst thou make men to live eternally
> Or, being dead, raise them to life again,
> Then this profession were to be esteemed."

It was thoughts like this which led Dr. Faustus straight to the devil saying "Physic farewell." Is not the pursuit of a "universal cancer cure" dangerously near to the desire to be "a sound magician" and "a mighty god"? This is for the quacks, a few of whom are no less earnest and well-meaning than we are, but who nevertheless impose on the pitiful anxiety of the public, supported by an ill-advised press at times and quite often sustained by doctors who see and know little of the fine variability of growth disorders, and who, by endorsing their spurious remedies, monotonously expose their own inexperience as one after another they announce that they have never seen anything like it happen before. Credulity, in many fields other than medicine, is due less to lack of brains than to lack of knowledge; it is often easier to fool the intellectual when he is out of his depth than it is to take in the illiterate.

The necessity for cancer treatment is an indication of our failure to prevent, or marks the limit of our ability to postpone; and treatment itself is designed to keep a man healthy for his normal span of life if that be possible and to relieve his suffering if it be not. This seems to me to be the very stuff and heart of medicine, just as universal cures are the stock-in-trade of magicians. Sir William Jenner said that the three essential qualities of a doctor were that he must be honest, that he must be dogmatic, and that he must be kind; he did not say that he must work miracles. Familiarity with the advances that have been made in the knowledge of cancer, and of the effects produced by the treatment methods that are used, will help us to offer our patients the best advice and treatment that is procurable for them at the time. A close study of each individual, to assess both the activity and degree of advancement of the disease and the particular suffering, mental and physical, which that patient is experiencing, will help us to decide what we want to achieve. The difficult things that sound so simple, like a clear idea both of what we want to do and what is possible, are more likely to lead to progress in the treatment of breast cancer than the easy things that sound so grand, like either sitting waiting for someone else to find "a cure" or reassuring ourselves that what we have always done is still the best.

Bibliography at foot of next column

SURVIVAL OF TRANSFUSED RED CELLS
PREVIOUSLY STORED FOR LONG PERIODS IN THE FROZEN STATE

P. L. MOLLISON, M.D. Camb., M.R.C.P.
H. A. SLOVITER*, M.D., Ph.D. Pennsylvania
H. CHAPLIN, JUN.†, M.D. Columbia

From the Blood Transfusion Research Unit, Postgraduate Medical School of London, and National Institute for Medical Research, Mill Hill, London

RED cells in 15% glycerol can be frozen and thawed with the production of only slight hæmolysis (Smith 1950). The glycerol can be removed from such cells by dialysis, and the recovered red cells can then be used for transfusion (Sloviter 1951). Human red cells, recovered in this way after having been kept at −79°C for two hours, survive normally in the recipient after transfusion (Mollison and Sloviter 1951). Red cells stored at −79°C for up to eight months appear normal (Sloviter 1952a), and it is shown here that such red cells survive normally after transfusion.

In a study of the behaviour of red cells at temperatures between 0°C and −79°C it was found that a considerable proportion of the red cells could be recovered after storage in 15% glycerol at −15°C for several weeks (Sloviter 1952b). The percentage of red cells which can be recovered after storage at −15°C is much lower than after storage at −79°C. Nevertheless transfusion experiments were made to determine whether −15°C is a sufficiently low storage temperature to prevent those changes (presumably due to metabolic activity) which shorten the survival of the red cell after transfusion. The results show that red cells recovered after storage at −15°C for eighty days have an approximately normal survival in vivo.

METHODS

Storage of Blood

Pilot tubes obtained at a routine blood collection of the National Blood Transfusion Service were tested and bottles of group-A type-N blood selected. The bottles of blood had been stored for three or four days at +4°C by the time they were selected. Before mixing with the glycerol solution, about 150 ml. of plasma was removed to prepare a concentrated suspension of red cells. The procedure for freezing and recovery of the red cells was exactly the same as that described by Mollison and Sloviter (1951), except that the red cells were stored at −79°C (solid carbon dioxide-alcohol) for periods up to eight months. As before, the red cells were transfused seven or eight days after thawing; this delay was due mainly to making sterility tests on the red-cell suspensions before transfusion.

* American Cancer Society fellow, 1951–52, awarded on recommendation of the Committee on Growth of the National Research Council.
† U.S. Public Health Service research fellow, and, more recently, senior assistant surgeon, U.S. Public Health Service (Res.).

PROF. D. W. SMITHERS: BIBLIOGRAPHY

Berven, E. (1949) *Amer. J. Roentgenol.* **62**, 320.
Engelstad, R. B. (1942) *Acta chir. scand.* **87**, 545.
— (1948) *Amer. J. Roentgenol.* **60**, 776.
Evans, W. A., Leucutia, T. (1939) *Ibid*, **42**, 866.
Foulds, L. (1951) *Ann. R. Coll. Surg.* **9**, 93.
Haagensen, C. D., Stout, A. P. (1942) *Ann. Surg.* **116**, 801.
— (1949) *Amer. J. Roentgenol.* **62**, 352.
Handley, R. S. (1952) *Proc. R. Soc. Med.* (in the press).
— Thackray, A. C. (1949) *Lancet*, ii, 276.
Kaae, S. Cited by Neilsen (1951).
McWhirter, R. (1948) *Proc. R. Soc. Med.* **41**, 122.
— (1950) *Brit. J. Cancer*, **4**, 368.
Neilsen, J. (1951) Transactions of the 25th meeting of the Northern Surgeons Association. Copenhagen.
Nohrman, B. A. (1949) *Acta radiol. Stockh.* suppl. no. 77.
Richards, G. E. (1948) *Brit. J. Radiol.* **21**, 109.
Smithers, D. W., Rigby-Jones, P., Galton, D. A. G., Payne, P. M. (1952) *Ibid*, suppl. no. 4.
Taylor, G. W. (1949) *Amer. J. Roentgenol.* **62**, 3.
Truscott, B. McN. (1947) *Brit. J. Cancer*, **1**, 129.
Windeyer, B. W. (1949) *Amer. J. Roentgenol.* **62**, 345.

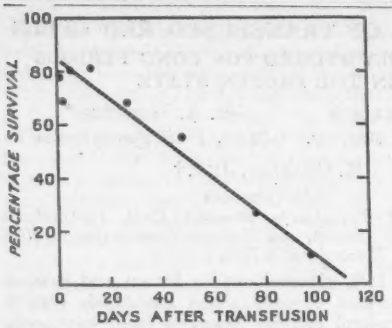


Fig. 1—Survival after transfusion of red cells stored at −79°C for three months and at +4°C for eleven days (case 1).

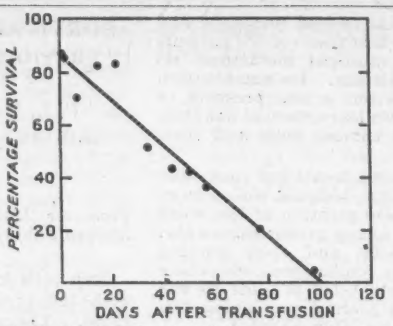


Fig. 2—Survival after transfusion of red cells stored at −79°C for six months and at +4°C for eleven days (case 2).

In further experiments blood was stored at −15°C. In these experiments the procedure was similar, except that the blood-glycerol mixture was simply placed in an ordinary deep freezing cabinet and in some instances solidified quite slowly (many hours). Thawing was carried out by placing the bottles in a water-bath at +37°C. Thereafter the procedure was the same as for blood stored at −79°C.

In the present work the volume of red cells frozen was determined by measuring the volume and hæmatocrit of the original suspension; and this was compared with the final volume of red cells recovered after freezing, thawing, dialysis, and washing. Thus the estimations of the percentage recovery of red cells include losses during dialysis and washing.

Control Blood

On the day of transfusion a donor of group O, type M, was obtained and blood was drawn into acid-citrate-dextrose about an hour before the time arranged for transfusion. A and B substance (Sharp & Dohme) was added in the proportion of 1 ml. to every 50 ml. of blood to reduce the anti-A activity of the donor plasma.

Choice of Recipients

Ten patients were transfused, each receiving both stored (previously frozen) and fresh (control) red cells. All the patients belonged to group A (Rh-positive) and were M-positive. All but one of the patients were women, and most of them had iron-deficiency anæmia connected with pregnancy.

Measurement of Survival of Transfused Red Cells

The concentration of surviving cells was estimated by differential agglutination, Dacie and Mollison's (1943) modification of Ashby's method being used. The method was further modified because of the rather small quantities of red cells transfused in some experiments. The modification consisted simply in using a more concentrated suspension of red cells, so that the final concentration of blood in the tests (after adding the agglutinating serum) was 1 in 42. For counts of O cells highly potent anti-A sera produced in rabbits were used; for counts of N cells anti-M powdered globulin (Lederle) was used (Ebert and Emerson 1946).

"Blank" (pre-transfusion) counts with anti-A serum were 4000–11,000 cells per c.mm. in nine cases, and 21,000 in the remaining case; with anti-M sera the blank counts were all between 2000 and 7000 cells per c.mm. On the day after transfusion the counts of previously frozen cells were 128,000–254,000 per c.mm. in eight cases, and 67,000 and 478,000 per c.mm. in the remaining two. Counts of control cells were higher; 126,000–280,000 per c.mm. in five cases, and 408,000–862,000 per c.mm. in the remaining three.

For each population of transfused cells, estimates on the day after transfusion were based on counts of 4000 cells; most other estimates were based on counts of 2000 cells; but, when very few cells were left, only 1000 cells were counted.

The volume of cell suspension transfused was measured by weighing the bottle with its contents before and after transfusion and determining the specific gravity of the blood mixture. Any cell suspension left in the giving set was returned to the bottle before the final weighing.

The red-cell count of a well-mixed sample from each bottle was determined by counting not less than 4000 red cells. From these data the "expected" ratio of test cells to control cells was calculated—i.e., the ratio expected if the previously frozen and the freshly drawn red cells survived equally well. For convenience the ratios actually found have in each case been expressed as percentages of the expected ratio (see table I).

These "percentage survivals" express simply the survival of the stored cells relative to the control cells; thus, "100% survival" implies that the stored cells are surviving exactly as well as the control cells, and not that all the stored cells are surviving.

The absolute percentage survival was estimated in the following way. First, the concentration of test cells expected on the day after transfusion, if the test cells survived just as well as the control cells, was:

$$\text{Observed count of control cells, Day}_1 \times \frac{\text{No. of test cells transfused}}{\text{No. of control cells transfused}}$$

This figure was considered as 100% survival of the test cells, and the observed count of test cells on any day

TABLE I—PROTOCOL OF CASE 2

(The method of obtaining the figures in columns 4–8 is described in the text)

(1) Days after transfusion	(2) Test (prev. frozen) red cells (×10³ per c.mm.)	(3) Control (fresh) red cells (×10³ per c.mm.)	(4) Observed ratio: test / control	(5) Ratio observed / Ratio expected (%)	(6) % Survival of test cells (uncorrected)	(7) "Expected" counts of control cells (×10³ per c.mm.)	(8) "Absolute" survival of test cells (%)
1	123	136	0·91	87	87	136	87
2	120	137	0·88	84	85	135	83
7	100	127	0·79	76	70	128	71
15	116	135	0·86	82	82	119	73
22	117	126	0·93	89	83	111	66
34	72	93	0·78	75	51	97	53
43	61	74	0·83	80	43	87	51
50	60	67	0·90	86	42	79	50
56	51	58	0·88	84	36	72	44
77	28	31	0·90	86	20	49	31
98	6	8	—	—	4	25	13
119	3	—	—	—	—	—	—

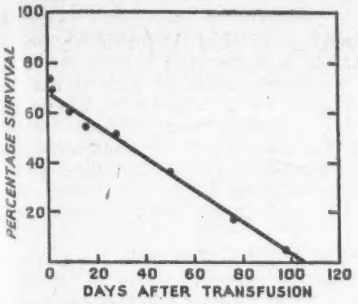


Fig. 3—Survival after transfusion of red cells stored at −79°C for six months and at +4°C for ten days (case 3).

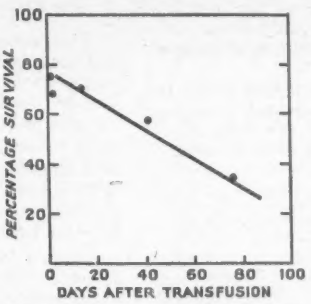


Fig. 4—Survival after transfusion of red cells stored at −79°C for six months and at +4°C for eleven days (case 4).

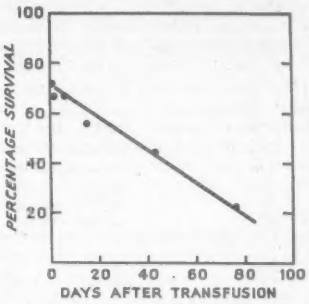


Fig. 5—Survival after transfusion of red cells stored at −79°C for six months and at +4°C for ten days (case 5).

(Day_n) could then be expressed as a percentage of this figure.

A correction for fluctuations of plasma volume was made by taking into account the difference on any day between the observed count of control cells and that expected if their number decreased by exactly $^1/_{110}$ a day. (All but one of the recipients were female: in the one male recipient a loss rate of $^1/_{120}$ a day was assumed.) The expected count of control cells on Day_n is thus:

$$\text{Count of control cells, Day}_1 \times \frac{(110 - n)}{110}$$

where n = no. of days after transfusion

Thus an estimate of the absolute survival of the test cells on Day_n, as a percentage, is given by the formula:

$$\frac{\text{Observed count of test cells, Day}_n}{\text{Count of test cells equiv. to 100\% survival}} \times \frac{\text{Expected count of control cells, Day}_n}{\text{Observed count of control cells, Day}_n} \times 100$$

RESULTS

Clinical Observations

No febrile reactions were noted after the transfusions. One of the patients developed transient mild urticaria, but in the remainder no untoward effects were observed.

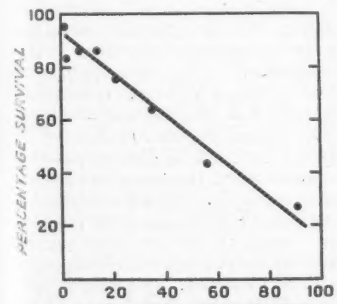


Fig. 6—Survival after transfusion of red cells stored at −15°C for seventy-seven days and at +4°C for ten days (case 9).

Loss of Red Cells during Storage and "Processing"

As previously reported, experiments with small quantities of red cells stored at −79°C have shown that the proportion of red cells recovered after thawing diminishes with time (Sloviter 1952a). In the present experiments with larger quantities of red cells the amount of red cells recovered after storage and processing was in most cases about 50% of the amount originally frozen. There were considerable variations between one batch and another. For example, in the present series the best yield (80%) was obtained from the blood which had been stored the longest time (eight to nine months). Hæmolysis is much greater after storage at −15°C than at −79°C. Thus after twenty-nine days at −15°C the yield was about 50%, and after eighty days about 20%. It must be emphasised that the data presented above relate only to recoveries of cells before transfusion and bear no relation to the results presented below, which deal with the survival in the circulation of those red cells which were transfused.

Survival of Red Cells in Vivo

To illustrate the method of calculation of results, the full protocol of a case is set out:

Case 2.—A man, aged 49, had severe hypochromic anæmia secondary to previous bleeding from gastric ulcer. Hb 6·4 g. per 100 ml. Blood group A, type M. Transfused with previously frozen red cells and with freshly drawn red cells.

Previously frozen red cells.—Group-A type-N blood drawn from donors on June 2, 1951; kept at + 4°C till June 5; then frozen and kept at − 79°C till Dec. 4; then thawed; cells recovered in the usual way and held at + 4°C till Dec. 12, 1951; then transfused. Amount transfused: 275 ml.; red-cell count 2,680,000 per c.mm.

Fresh red cells.—Group-O type-M blood drawn from donor one hour before transfusion; AB substance added. Amount transfused: 227 ml.; red-cell count 3,110,000 per c.mm.

Expected ratio of surviving cells:

$$\frac{\text{No. of test cells transfused}}{\text{No. of control cells transfused}} = \frac{275 \times 2{\cdot}68}{227 \times 3{\cdot}11} = 1{\cdot}044$$

Blank counts.—Before transfusion, when a suspension of the patient's red cells was mixed with an anti-A serum, all but 4000 red cells per c.mm. were agglutinated; with an anti-M serum all but 2000 red cells per c.mm. were agglutinated. These "blank" counts have been subtracted from the results which follow.

Ratio found, Day_1 (see column 4, table I):

$$\frac{\text{Count of test cells, Day}_1}{\text{Count of control cells, Day}_1} = \frac{123{,}000}{136{,}000} = 0{\cdot}91$$

Relative percentage survival, Day_1 (see column 5, table I):

$$\frac{\text{Ratio found, Day}_1}{\text{Ratio expected}} = \frac{0{\cdot}91}{1{\cdot}044} \times 100 = 87\%$$

Count of test cells expected on Day_1, if 100% survived:

$$\text{Count of control cells, Day}_1 \times \text{"Expected ratio"} \left(\text{i.e., } \frac{\text{No. of test cells transfused}}{\text{No. of control cells transfused}}\right)$$

i.e., $136{,}000 \times 1{\cdot}044 = 142{,}000$ per c.mm.

Absolute survival of test cells, Day_{50}, uncorrected (see column 6, table I):

$$\frac{\text{Observed count of test cells, Day}_{50}}{\text{Expected count of test cells, Day}_1} = \frac{60{,}000}{142{,}000} = 42\%$$

Expected count of control cells, Day_{50} (see column 7, table I):

$$\text{Count of control cells, Day}_1 \times \frac{120-50}{120} = 136{,}000 \times \frac{70}{120} = 79{,}000$$

Absolute survival of test cells, Day_{50}, corrected (see column 8, table I):

$$\text{Observed survival test cells, Day}_{50} \times \frac{\text{Exp. count control cells, Day}_{50}}{\text{Obs. count control cells, Day}_{50}}$$

$$= 42 \times \frac{79{,}000}{67{,}000} = 50\%$$

Further results are set out in table II and figs. 1–6.

To consider first the post-transfusion survival of red cells stored at −79°C relative to the survival of the

TABLE II—SURVIVAL OF PREVIOUSLY FROZEN RED CELLS AT VARIOUS TIMES AFTER TRANSFUSION, EXPRESSED AS A PERCENTAGE OF THE SURVIVAL OF A CONTROL POPULATION OF FRESHLY DRAWN RED CELLS

(No allowance has been made for the fact that the test cells were stored for 11 days at + 4°C whereas the control cells were freshly drawn; the values in this table should be increased by approximately 10% to allow for this)

Case	Length of storage	Survival of previously frozen red cells as a percentage of the survival of freshly drawn red cells at various intervals after transfusion						
		Immed.	1 day	2 days	6–9 days	13–16 days	35–56 days	76–91 days
	Stored @ −79°C							
1	3 months	93	78	71	79	92	96	89
2	6 months	93	87	84	76	82	83	86
3	6 months	78	73	69	66	65	62	56
4	6 months	88	75	70	..	80	90	110
5	6 months	85	72	69	71	66	72	73
6	3 months	..	92	90	..	..	..	..
7	8½ months	82	76	77	71	40	0	..
	Mean (Cases 1–7)		79·0	75·7				
	(Cases 1–5)	87·4	77·0	72·6	73·0	77·0	80·6	82·8
	Stored @ −15°C							
8	29 days	82	77	76	74	..	88	..
9	77 days	100	95	86	92	98	89	..
10	84 days	106	75	70	70	82	91	*
	Mean (Cases 8–10)	96·0	82·3	77·3	78·7	..	89·3	..

* Definite evidence of survival but number of cells too small for accurate estimation of ratio.

control red cells (see table II): immediately after transfusion survival was 78–93%, mean 87%; at twenty-four hours it was 72–92%, mean 79%; in six out of seven cases there was a slight further fall at forty-eight hours, with a mean survival of 76%. Thereafter there was no tendency to fall any further—i.e., the test cells were removed from the circulation at about the same rate as the control cells. In one exceptional case (case 7) both test and control cells were eliminated within sixty days of transfusion (see below).

In the three cases in which blood stored at −15°C was transfused the results were similar to those in blood stored at −79°C (table II). Survival fell from 96% immediately after transfusion to 82% at twenty-four hours, and to 77% at forty-eight hours. Thereafter there was no increased loss of previously frozen red cells relative to that of fresh red cells.

Estimates of the absolute survival of the stored cells in cases 1–5 and 9 are plotted in figs. 1–6. The method of correcting the observed values to obtain estimates for "absolute survival" has already been described. It will be seen that the estimates from forty-eight hours onwards fit straight lines cutting the time axis at about a hundred and ten days after transfusion.

In the one exceptional case (case 7) referred to above, the number of previously frozen red cells fell rather rapidly after about the first week, with the result that at fourteen days the percentage survival was much lower than that of the control. However, the next blood sample taken from the recipient, forty-two days after transfusion, showed that the fresh red cells were also disappearing rapidly; the survival of the previously frozen red cells was now nil, and that of the fresh red cells, relative to their initial concentration, was less than 10%. A sample taken two months after transfusion contained no transfused cells at all. It was now apparent that the abnormality lay in the recipient rather than in the donor, and that the case was very like those described by Loutit et al. (1943), of which some further details were given by Mollison (1951). It is not proposed to discuss the matter further at present, except to say that it seems clear that the rapid disappearance of the red cells in this case was not due to any effects of storage.

DISCUSSION

The post-transfusion survival of the previously frozen red cells is expected to be lower than that of the fresh red cells because the frozen red cells were stored for ten or eleven days at + 4°C in addition to the period of storage in the frozen state. From previous work it may be estimated that the red cells of blood stored in acid-citrate-dextrose for ten or eleven days have about a 90% survival at twenty-four hours after transfusion (Gibson et al. 1947, Ross et al. 1947, Mollison and Sloviter 1951).

Another factor which would tend to make the survival values for the previously frozen cells low was the presence of an appreciable number of "ghosts" in the suspension of red cells transfused. These ghosts are not completely removed during the washing of the recovered cells after dialysis. In the present work, in determining the number of previously frozen red cells in the suspension prepared for transfusion, all red cells were counted even when they were ghost-like. It was estimated that less than 5% of the cells were ghosts.

When allowance is made for these two factors (eleven days' storage at + 4°C and the presence of ghosts), it is evident that the expected survival of the previously frozen red cells is about 85%, if storage in the frozen state has had no deleterious effect on the cells. The survival of the frozen cells at forty-eight hours after transfusion was in fact 70–90%. It seems therefore that very little, if any, irreversible change takes place during storage at −79°C in those cells which escape lysis. There is good reason to believe that the lysis which occurs during storage and processing is due to physical rather than biochemical processes. Biochemical activity at −79°C is expected to be negligible; and this belief is supported by the observation that those previously frozen red cells which are present in the circulation forty-eight hours after transfusion are capable of a normal life-span. As figs. 1–6 show, the estimates from forty-eight hours onwards, when plotted against time, fall on straight lines cutting the time axis at about a hundred and ten days.

The advantage of comparing the survival of one population of red cells with another is well illustrated by case 2 (table I). During the first twenty-two days after transfusion there was no apparent decrease in the survival of either population, owing presumably to shrinkage of the recipient's plasma volume. Confidence in the validity of the results is greatly increased by showing that the survival of one population relative to the other remained constant both during this period and during the subsequent period when the concentration of both populations started to diminish. In the present series it was particularly important to have a control population of red cells, since many of the recipients were recently delivered women in whom considerable changes of plasma volume were to be expected. The advantages of a control population are further illustrated by case 7: in this case the bad survival of the previously frozen red cells might have been ascribed to damage during freezing, had it not been possible to show that the same recipient rapidly destroyed fresh red cells.

It is a very interesting feature of the results obtained with red cells stored at −15°C that, although relatively few red cells were recovered after storage, these were capable of a normal life-span. Evidently, if appreciable ageing of the red cells took place at −15°C, cells recovered after storage for eighty days would be expected to be incapable of surviving for as long as a hundred days after transfusion. In fact, as clearly illustrated in fig. 6, those cells which are present in the recipient's circulation twenty-four hours after transfusion disappear at a rate indistinguishable from that of fresh red cells.

Practical Value of Storing Red Cells in Frozen State

At present there are two main obstacles to be overcome before storage of red cells in the frozen state can be of practical value in the field of blood-transfusion. First, a simpler and less time-consuming method for the removal of glycerol from the red cells must be devised, because the technique used in these studies is too cumbersome for general use. The process recently described by Lovelock (1952) may be the answer to this problem. Secondly, a higher recovery of red cells after storage at −79°C must be attained before the expense of storage at this low temperature can be justified. At present, after storage at −79°C for several months the recovery may be as low as 50%, and is even lower after storage at −15°C. However, recent work suggests that it may be possible to improve these yields considerably (Chaplin 1952).

The most important conclusion from the present work is that red cells recovered after storage at low temperatures have a normal post-transfusion survival. Therefore, if the number of cells destroyed by physical processes can be reduced, it may become worth while to store red cells in the frozen state for long periods.

SUMMARY

Human red cells stored in 15% glycerol at −79°C for six months are capable of normal survival after transfusion. When they are stored at −15°C for about eighty days, only a small proportion of the red cells can be recovered after thawing; however, these also have a normal post-transfusion survival. The implications of these observations are discussed.

It is a pleasure to thank Sir Charles Harington, F.R.S., and the Medical Research Council for hospitality to one of us (H. A. S.) at the National Institute for Medical Research; Mr. A. S. Parkes, SC.D., F.R.S., for his continued interest and advice; and Dr. A. A. Miles for his generous help on the bacteriological aspects of the present work. Prof. J. McC. Browne kindly allowed us to make observations upon patients in the department of obstetrics, Hammersmith Hospital, and Dr. J. D. James, director of the North London Blood Supply Depot, again arranged for a supply of suitable donors. We are very grateful to Miss Hal Crawford, B.SC., and Miss Marie Cutbush, B.SC., for much help, particularly in doing a great many of the Ashby counts; and to Miss Rita Lyons for skilful assistance in the freezing and processing of the blood.

REFERENCES

Chaplin, H. (1952) To be published.
Dacie, J. V., Mollison, P. L. (1943) *Lancet*, i, 550.
Ebert, R. V., Emerson, C. P. jun. (1946) *J. clin. Invest.* **25**, 627.
Gibson, J. G., Evans, R. D. Aub, J. C., Sack, T., Peacock, W. C. (1947) *Ibid*, **26**, 715.
Loutit, J. F., Mollison, P. L., Young, I. M. (1943) *Quart. J. exp. Physiol.* **32**, 183.
Lovelock, J. E. (1952) *Lancet*, i, 1238.
Mollison, P. L. (1951) Blood Transfusion in Clinical Medicine. Oxford.
— Sloviter, H. A. (1951) *Lancet*, ii, 862.
Ross, J. F., Finch, C. A., Peacock, W. C., Sammons, M. E. (1947) *J. clin. Invest.* **26**, 768.
Sloviter, H. A. (1951) *Lancet*, i, 1350.
— (1952a) *Nature, Lond.* **169**, 1013.
— (1952b) Unpublished observations.
Smith, A. U. (1950) *Lancet*, ii, 910.

"The Long Vacation is becoming in Cambridge an increasingly busy academic period, so much so that it is popularly, and quite improperly, known as the 'Long Vac. Term.' . . . it is a bad organisation of studies which would turn vacation into term; and it presses hardly upon that hard-pressed creature, the teaching don. It is a vivacious myth, that a don has leisure. He has not—the 'older model' don at least, who actually taught as well as studied and who was a characteristic of the older English universities. The chief importance of the Long was that it made possible his way of life. That it should continue to be possible is vital, for it will be catastrophic if the University is broken up into castes of persons who teach, who research and who administer, each of them exclusively."—*Manchester Guardian*, Sept. 3, 1952, p. 4.

OBSERVER ERROR IN THE INTERPRETATION OF CHEST FILMS*

AN INTERNATIONAL INVESTIGATION

A. L. COCHRANE M.B. Camb., D.P.H.
L. H. GARLAND M.D.

From the Pneumoconiosis Research Unit of the Medical Research Council, Llandough Hospital, near Cardiff; and Stanford University, U.S.A.

DURING the last five years there has been an increasing interest in methods of measuring, and if possible reducing, the effect of observer error in fields where its existence had previously been ignored. In particular this is true of medicine, although only in the radiological diagnosis of pulmonary tuberculosis, on miniature and on full-sized chest films, has a detailed investigation been made, and this has been done almost exclusively in the United States. It was clearly shown that radiologists and chest physicians, however well trained, show a considerable inter-observer and intra-observer error (Birkelo et al. 1947, Garland 1949, Yerushalmy et al. 1950). As a result, techniques for reducing these errors were found. It is surprising that this work has evoked so little attention in Great Britain. Recent figures suggest that in British mass miniature radiography the observer error should be studied and techniques for its reduction applied (Stewart and Hughes 1951).

In the measurement of observer error in the diagnosis of other respiratory diseases in chest films the British have been the pioneers. Fletcher and Oldham (1949) have noted how physicians varied in their interpretation of coalminers' films. This naturally led the film readers in the Pneumoconiosis Research Unit to treat their diagnosis of tuberculosis with some suspicion. The American work gave additional cause for anxiety, and it was decided, as a preliminary step, to find out how British observer error compared with the American by reading a short series of films which contained an unknown proportion showing reinfection-type tuberculosis. The British readers had every reason to fear the comparison with their American colleagues, and they were therefore pleasantly surprised to find that their errors were rather less than those published in the United States (Cochrane 1951). It was thought that this might be because the films were easier to interpret than those used by the Americans. Later, it was possible for the British films to be read by some of the American investigators.

* A similar paper is to be published in the U.S.A. in the near future.

TABLE Ia—AMERICAN READERS; DISTRIBUTION OF FILMS ACCORDING TO TUBERCULOSIS CLASSIFICATION

Reader	Tuberculosis positive					Tuberculosis negative
	Active	Inactive			Total	
		Clinically significant	Not clinically significant	Total		
A_1 1st reading	20	3	12	15	35	54
2nd ,,	17	6	8	14	31	58
A_4 1st ,,	26	0	9	9	35	54
2nd ,,	23	1	9	10	33	56
A_2 1st ,,	18	..*	..	10	28	61
2nd ,,	20	..	..	10	30	59
Mean	20·7	2·5†	9·5†	11·3	32·0	57·0
Range	17–26	0–6	8–12	9–15	28–35	54–61

* Reader A_2 did not indicate clinical significance.
† Excluding reader A_2.

TABLE I*b*—BRITISH READERS; DISTRIBUTION OF FILMS ACCORDING TO TUBERCULOSIS CLASSIFICATION

Reader	Tuberculosis positive					Tuberculosis negative
	Active	Inactive			Total	
		Clinically significant	Not clinically significant	Total		
B_1 1st reading	11	11	12	23	39	55
2nd ,,	12	6	10	16	28	61
B_2 1st ,,	19	3	2	5	24	65
2nd ,,	18	5	6	11	29	60
B_3 1st ,,	17	4	7	11	28	61
2nd ,,	17	4	8	12	29	60
B_4 1st ,,	20	5	2	7	27	62
2nd ,,	20	7	2	9	29	60
B_5 1st ,,	5	13	3	16	21	68
2nd ,,	5	14	2	16	21	68
B_6 1st ,,	11	9	3	12	23	66
2nd ,,	8	9	7	16	24	65
Mean	13·6	7·5	5·3	12·8	26·4	62·6
Range	5–20	3–14	2–12	5–23	21–34	55–68

The original set of films was not selected with an exhaustive study in view. A short trial was prepared with the simple objective of comparing directly British and American observer error, and in this it was successful. This paper is presented as a report of these findings.

MATERIAL AND TECHNIQUE

The films used for the trials were 14 × 17 in. survey chest films, taken by a mobile unit on a radiography survey, which were very generously put at our disposal by Dr. Norman Tattersall, then medical director of the Welsh National Memorial Association. We asked Dr. Tattersall to provide about 100 chest films of good technical quality, of which between 5 and 30 should show some sign of reinfection-type tuberculosis. From these, 89 films were selected by another doctor, who did not take part in the trial, as technically adequate, and as containing a suitable proportion of films showing minimal disease. Six readers (see Appendix A) then indicated their interpretation on a prepared form (see Appendix B) so arranged that a comparison would be possible of the relative reproducibility of classifications based on the diagnosis of "active" tuberculosis and of "clinically significant"† tuberculosis. Readings were made on two separate occasions and were strictly supervised. The films were then mailed to San Francisco, where three members of the Chest Radiological Research Committee read the films under similar conditions. Both sets of results were analysed in San Francisco and at the Pneumoconiosis Research Unit; the analyses were then exchanged, and agreement was reached on the basic conclusions.

Contact between the two groups was made when Dr. C. M. Fletcher, director of the Pneumoconiosis Research Unit, visited San Francisco in March, 1950, and Dr. L. H. Garland, chairman of the Chest Radiological Research Committee, visited the research unit in Cardiff in August, 1950. It became clear, in retrospect of course, that contact would have been more valuable before the readings than after. For instance, the Americans interpreted the phrase "clinically significant" differently from the British, and this would have been avoided by previous discussion.

TABLE II*a*—AMERICAN READERS; AVERAGE AND RANGE OF "AGREEMENT" AND "DISAGREEMENT" (SEE TEXT) IN PRESENCE OF TUBERCULOSIS

—	Agreement on presence of tuberculosis	Agreement on absence of tuberculosis	Disagreement	Disagreement as % of all films	Disagreement as % of films called positive at least once
Between pairs of readers (inter-individual)	26·7 (24–32)	50·3 (50–51)	12·0 (6–15)	13·5 (6·7–16·9)	31·0 (15·8–38·5)
Between readings of individuals (intra-individual)	29·7 (27–31)	54·7 (52–58)	4·7 (4–6)	5·2 (4·5–6·7)	13·6 (11·4–16·2)

† A film is classified as showing "clinically significant" tuberculosis if, in the opinion of the observer, the shadows in the film are such that he would recommend immediate medical action or that the subject should return for a second film in less than six months. Thus the definition can include films which would be classified as "inactive" in a simple "active/inactive" dichotomy.

ANALYSIS

A convenient way of measuring disagreement is to take each pair of readers in turn and to enumerate the films on which they agreed and disagreed. The number of films on which there was disagreement, averaged over all possible pairs of readers (15 if there are six readers), may be called the mean disagreement of the group, and it can be expressed as a percentage of either the total number of films or the total of films that were called positive by at least one reader.

TABLE II*b*—BRITISH READERS; AVERAGE AND RANGE OF "AGREEMENT" AND "DISAGREEMENT" (SEE TEXT) ON PRESENCE OF TUBERCULOSIS

—	Agreement on presence of tuberculosis	Agreement on absence of tuberculosis	Disagreement	Disagreement as % of all films	Disagreement as % of films called positive at least once
Between pairs of readers (inter-individual)	22·7 (21–27)	59·4 (53–66)	6·9 (2–13)	7·7 (2·2–14·6)	23·2 (8·7–38·2)
Between readings of individuals (intra-individual)	24·5 (21–27)	60·7 55–68)	3·8 (0–8)	4·3 (0–9)	13·5 (0–22·9)

Intra-individual disagreement is measured similarly by classifying the pairs of readings by each reader into agreements and disagreements, averaging the disagreements over all the readers, and expressing the results as a percentage of either the total number of films or the total number of films called positive at least once. Evaluation of disagreements in assessment of activity is made in an identical manner. Tables I*a*, II*a*, and III*a* show the results for the American readers, and tables I*b*, II*b*, and III*b* for the British readers.

RESULTS

British readers called a smaller proportion of the films positive for tuberculosis than did the American readers, the mean being 26·4 positives for the British and 32·0 for the Americans (tables I*a* and I*b*). Similarly the British read "active tuberculosis" in 13·6 of films on the average, whereas the Americans placed an average of 20·7 films in this category. However, more "inactive but clinically significant" cases were reported by the British than by the Americans. The mean number of "negative for tuberculosis" cases found by the British readers was 62·6, compared with 57·0 by the Americans.

In conferences between representatives of the two groups, held first in San Francisco and subsequently in Cardiff, it became apparent that American readers tended to emphasise minimal abnormal shadows to a greater extent than did British readers. This may be due to the

TABLE IIIa—AMERICAN READERS; AVERAGE AND RANGE OF "AGREEMENT" AND "DISAGREEMENT" (SEE TEXT) ON ACTIVITY OF TUBERCULOSIS IN FILMS IN WHICH TUBERCULOSIS IS AGREED TO BE PRESENT

—	No. of films agreed to show tuberculosis	Agreement on activity of tuberculosis	Agreement on inactivity of tuberculosis	Disagreement	Disagreement as % of no. agreed to show tuberculosis	Gross disagreement: active tuberculosis v. tuberculosis absent
Between pairs of readers (inter-individual)	26·7 (24–32)	17·3 (16–20)	3·7 (1–7)	5·7 (5–7)	21·2 (15·6–29·2)	2·3 (1–5)
Between readings of individuals (intra-individual)	29·7 (27–31)	19·0 (17–23)	8·7 (7–12)	2·0 (1–3)	6·7 (3·2–11·1)	1·3 (1–2)

TABLE IIIb—BRITISH READERS; AVERAGE AND RANGE OF "AGREEMENT" AND "DISAGREEMENT" (SEE TEXT) ON ACTIVITY OF TUBERCULOSIS IN FILMS IN WHICH TUBERCULOSIS IS AGREED TO BE PRESENT

—	No. of films agreed to show tuberculosis	Agreement on activity of tuberculosis	Agreement on inactivity of tuberculosis	Disagreement	Disagreement as % of no. agreed to show tuberculosis	Gross disagreement: active tuberculosis v. tuberculosis absent
Between pairs of readers (inter-individual)	22·7 (21–27)	8·9 (3–17)	4·9 (2–10)	8·9 (4–15)	39·3 (17·4–71·4)	0·9 (0–2)
Between readings of individuals (intra-individual)	24·5 (21–27)	12·0 (4–18)	9·8 (5–15)	2·7 (1–5)	10·9 (4·2–22·7)	0·5 (0–1)

fact that the three American readers had previously conducted extensive studies on minimal pulmonary lesions and had become aware of the potential significance of very small and faint shadows, especially in surveys of groups, such as nurses and medical students. Conversely, in a comparable but unpublished joint study of some films of coalminers, the British readers would interpret certain minimal radiological changes as "category 1 pneumoconiosis," whereas the American readers tended to report such films as "negative—within normal limits." In this instance the British observers had been conducting extensive surveys on coalminers, and therefore were on the alert for minimal parenchymal alterations which may later develop into definite pneumonoconiosis.

The mean number of inter-individual disagreements on "tuberculosis present" for the British readers in their first set of readings was 7·7% of all the 89 films, or 23·2% of those films which were ever read as showing tuberculosis (table IIb). These figures are lower than those obtained from the American readings, which were 13·5% and 31·0% respectively (table IIa). The intra-individual comparisons, however, were about the same in both groups. The American readers showed inconsistency between their first and second readings on 5·2% of the films, on the average, and the British figure was 4·3%.

Inter-individual disagreement on activity (first readings only) was surprisingly low, but higher for the British readers than for the Americans (tables IIIa and b). The mean number of disagreements on activity was 8·9, or 39·3% of the films agreed to show tuberculosis, for the British, compared with 5·7 or 21·2% for the Americans. The inter-individual disagreements were also somewhat greater for the British, with a mean of 2·7 or 10·9%, compared with 2·0 or 6·7% for the Americans. There were fewer complete disagreements—i.e., one reader reporting "active tuberculosis" while the other reported "tuberculosis absent"—by the British readers; the average was 0·9 for such disagreements for pairs of readers and 0·5 comparing each reader with himself. The corresponding American figures were 2·3 and 1·3.

It is a point of interest for British readers that the observer error, when the films are classified on the one hand as "clinically significant" including "active" and "inactive, but clinically significant," and on the other hand as "inactive," is much less than when they are classified simply as "active" and "inactive." This does not hold for American readers, and the reason for this finding among the British readers is obscure; but, if it holds generally in Britain, the adoption of this method of classification might assist in introducing some order into the present chaos in the field of tuberculosis terminology, as well as helping to achieve consistent and

TABLE IV—ANALYSIS OF FILMS ON WHICH BRITISH AND AMERICAN READERS DISAGREED

Film no.	Readings during trial (1st and 2nd occasions)		Comments at joint conference*	Conclusion
	British readers	American readers		
1	12 tuberculosis negative†	3 tuberculosis negative; 3 tuberculosis positive, inactive	Questionable small scar at right first space, laterally (A), negative (B)	Understandable difference of opinion on significance of a small opacity; no major disagreement
2	12 tuberculosis negative	2 tuberculosis negative; 4 tuberculosis positive, inactive	Questionable density right first space, laterally (A), negative (B)	No major disagreement
3 & 4	12 tuberculosis negative	2 tuberculosis negative; 4 tuberculosis positive, inactive (calcified hilar nodes)	Calcified nodes (A), negative (B)	No major disagreement; American readers coded the nodes; British did not
5	6 tuberculosis negative; 3 tuberculosis positive, active; 2 tuberculosis positive, inactive but clinically significant; 1 tuberculosis positive, inactive, not clinically significant	4 tuberculosis negative; 1 tuberculosis positive, active; 1 tuberculosis positive, inactive	Faint opacity left first space, possibly active (A), possible lesion (B)	Difficult case with probable minimal lesion and inevitable difference of opinion among different observers; both groups of readers diverged; no significant international disagreement
6	9 tuberculosis negative; 2 tuberculosis positive, active; 1 tuberculosis positive, inactive, but clinically significant	1 tuberculosis negative; 2 tuberculosis positive; 2 tuberculosis positive, inactive, but clinically significant; 1 tuberculosis positive, inactive and not significant	Lesion, right second rib, dense and probably obsolete; adjacent lesion right second space, soft (active) (A); negative except for healed primary (B)	Difficult case with small soft lesion overshadowed by adjacent small dense one; subsequent review by independent British consultant reported "positive and significant"

* A, American; B, British. † That is, of 12 readings, all were recorded as negative.

reproducible diagnosis. A statistical argument in support of this conclusion is given in Appendix C.

In cross-comparison between British and American readers, first readings alone being used, it was found that of 52 cases called tuberculosis negative unanimously by the British, 42 were also called negative unanimously by the American readers, 6 were called tuberculosis positive by one American reader, and 4 were called tuberculosis positive by two American readers. The 6 films over which major disagreement was apparently occurring were subsequently studied at a joint conference at Cardiff, with the results outlined in table IV. In 5 cases there proved to be no major disagreement; in 1 case there was disagreement on the interpretation of a rather difficult lesion.

CONCLUSION

No considerable difference existed between American and British readers in the accuracy with which they read the films. The greater accuracy with which the series was read, compared with that found in earlier American trials, must have been due to the series as a whole being easier. On the whole it appears that the results of the more detailed American studies already published could be applied to the work of British readers. There is no doubt that the application of their findings would be entirely beneficial.

SUMMARY

Following American work on inter-observer and intra-observer errors in the radiological diagnosis of tuberculosis, a small-scale test of these errors was made by six British readers. Rather smaller errors were found than had been expected.

The films were then sent to a group of radiologists in the U.S.A. Their errors were of a similar magnitude to those of the British group.

The difference from previous results is most probably due to a rather easier group of films having been chosen, and it is concluded that observer error in the radiological diagnosis of tuberculosis should be reduced by application of the methods already fully developed in the United States.

We wish to thank the teams of readers who provided the data, and the statisticians who did the analyses, especially Mr. Oldham, who provided Appendix C.

REFERENCES

Birkelo, C. C., Chamberlain, W. E., Phelps, P. S., Schools, P. E., Zacks, D., Yerushalmy, J. (1947) *J. Amer. med. Ass.* **133**, 359.
Cochrane, A. L. (1951) Proceedings of the Conference on the Application of Scientific Methods to Industrial and Service Medicine, London, 1950; p. 36.
Fletcher, C. M., Oldham, P. D. (1949) *Brit. J. industr. Med.* **6**, 168.
Garland, L. H. (1949) *Radiology*, **52**, 309.
Stewart, A., Hughes, J. P. W. (1951) *Brit. med. J.* **i**, 904.
Yerushalmy, J., Harkness, J. T., Cope, J. H., Kennedy, B. R. (1950) *Amer. Rev. Tuberc.* **61**, 443.

Appendices

A.—COMPOSITION OF READER PANELS

The American group consisted of the following three radiologists:

L. H. Garland, M.D., clinical professor of radiology, Stanford University.

E. R. Miller, M.D., associate professor of radiology, University of California.

M. A. Sisson, M.D., clinical instructor in radiology, Stanford University.

The British group consisted of the following members:

L. R. West, M.D., M.R.C.P., consultant physician, Sully Hospital, South Wales.

K. J. Mann, M.D., M.R.C.P., D.P.H., member of the scientific staff of the Medical Research Council.

A. L. Cochrane, M.A., M.B., D.P.H., member of the scientific staff of the Medical Research Council.

V. H. Springett, M.D., Prophit scholar, Royal College of Physicians of London.

I. Davies, M.D., M.R.C.P., D.P.H., member of the scientific staff of the Medical Research Council.

T. W. Davies, B.SC., M.B., B.CH., D.P.H., consultant-chest physician to South Wales Regional Hospital Board.

B.—FORM USED FOR CLASSIFICATION OF FILMS

X-ray no.	*Tb absent*	*Tb present*	*Active*	*Inactive stable*	*Of clinical significance*
W5092405	+	..	..	..	..
W0060938	..	+	..	+	+
5091717	..	+	+	..	..
5091760	+	..	..	..	..
0123149	..	+	..	+	..
&c.					

Each observer was asked to place a mark in the appropriate column or columns opposite the reference number of each film.

C.—RELATIVE MERITS OF DIFFERENT WAYS OF READING TUBERCULOSIS

P. D. OLDHAM
M.A. Oxfd
MEMBER OF PNEUMOCONIOSIS RESEARCH UNIT

In the trial whose results are reported here the readers were required to classify each film under one of the following headings:

A, tuberculosis absent.
B, tuberculosis present, active, and clinically significant.
C, tuberculosis present, inactive, but of clinical significance.
D, tuberculosis present, but inactive and of no clinical significance.

It is more customary to divide films into only two classes, but there is disagreement about where the dividing line is to be drawn. It usually lies between one or other pair of the headings given above, and systems that have been used are three:

(1) tuberculosis present or absent (A or B, C, D).
(2) tuberculosis active or inactive (B or A, C, D).
(3) clinically significant or not significant tuberculosis (B, C or A, D).

The results obtained from the British readers can be used to throw some light on the relative merits of these three systems.

By means of the technique known as analysis of variance, numerical results in a table with multiple headings can be analysed to show the significance of average differences between the different headings. In a table giving the results of multiple tests given to multiple observers the analysis could break down the total variance of the observations into sections corresponding to differences between the observers, differences between the tests, and a remainder. The ratios of the first and second of these to the third represent a measure of the success of the first and second headings in explaining the variation of results throughout the table. If we were to apply this technique to the results obtained from the British readers, our subdivisions of the variance would correspond to differences between the six observers and differences between the 89 films, with a remainder. A large ratio between the first and third could indicate a large inter-observer error, and a large ratio between the second and third, large differences between films. Clearly we would like the results to make the first ratio small and the second large.

The results actually obtained were of course not numbers but the classification referred to as A, B, C, and D above. We can nevertheless carry out the analysis of variance procedure in algebraic terms, the subdivisions of the variance emerging as quadratic expressions in A, B, C, and D. The three possible groupings to be examined can then be introduced by putting

(1) $A = x$, and $B = C = D = y$,
(2) $B = x$, and $A = C = D = y$, and
(3) $B = C = x$, and $A = D = y$.

The observer-error ratio and the film-difference ratio can then be calculated for each suggested grouping in turn, and these ratios will not contain x and y. Thus we may at once examine the merits of the different groupings as revealed by the size of the ratios. They are:

	System 1	2	3
Observer error	7·93	16·74	6·44
Film differences .. .	56·50	22·04	65·80

It can be seen at once that system 2, corresponding to reading active tuberculosis only, is the worst. Systems 1 and 3 are very similar, but system 3 shows slightly smaller observer error and slightly better discrimination between different films. We may conclude that on the evidence of the British readings the best results would be obtained if films were classified on the basis of their clinical significance, though the system in which the criterion is the presence or absence of any kind of tuberculosis is almost equally good.

PRODUCTION OF HEPATITIS IN MICE BY THE COMBINED ACTION OF TWO FILTERABLE AGENTS

A. W. GLEDHILL, Ph.D. Camb., M.R.C.V.S.
G. W. A. DICK, M.D., B.Sc. Edin.
C. H. ANDREWES, M.D. Lond., F.R.C.P., F.R.S.
From the National Institute for Medical Research, Mill Hill, London

A PREVIOUS publication (Gledhill and Andrewes 1951) gave an account of the isolation from one strain of mice (P. mice) of a virus which caused fatal hepatitis in recently weaned mice of another strain, V.S. Rockefeller (Webster 1937). This mouse-hepatitis virus (M.H.V.) has been isolated from the blood and viscera of more than 50% of normal adult P. mice by 1–6 blind passes in just-weaned V.S. mice. Such passes were made at 7-day intervals with suspensions of liver and other viscera which were injected intraperitoneally. The disease in V.S. mice was prevented by aureomycin or terramycin when these were given not later than 48 hours after inoculation of the virus. Arising out of investigations into the action of terramycin in preventing mouse hepatitis, we made the rather bizarre discovery that the virus causing the disease could be resolved into two agents, each capable of being serially transmitted in susceptible mice. Either one alone rarely produced symptoms or lesions in the mice; yet together they gave rise to the typical disease. Mice infected either with the mixture or with the original M.H.V. died in 4–10—usually 5–7—days after infection when the dose was large. Their livers were necrotic, either uniformly yellow or, more often, strikingly mottled; their spleens were enlarged, the urine was dark, and there was sometimes visible jaundice. After smaller doses the liver damage might occur without death.

METHODS

The techniques used were similar to those described by Gledhill and Andrewes (1951) except that liver and spleen were used as the source of virus in place of liver and kidney. Suspensions and dilutions were made in 10% horse-serum broth with or without an equal volume of saline. The inoculum per mouse for all dilutions was 0·2 ml. given intraperitoneally. Terramycin (2 mg. per ml.) suspended in 5% gum acacia was given subcutaneously in a dose of 0·5 ml. V.S. mice weighing 8–10 g. were used for the experiments to be described.

RESULTS

Discovery of 'S.,' the Stable Component of M.H.V.

In our experiments with terramycin, we found that mice were protected by a single dose of the antibiotic given on the same day as a large dose of M.H.V. (more than 10^3 L.D.$_{50}$). Such a dose of terramycin had no effect when given 24 hours before the virus. It was next observed that mice treated with M.H.V. and terramycin on the same day became refractory to challenge with a large dose of M.H.V. 2 or more days later. In table I an experiment is recorded in which groups of mice were challenged with M.H.V. 1, 2, and 3 days after treatment with M.H.V. and terramycin on day 0; the controls of each group received terramycin only on day 0, followed by the challenge dose of M.H.V. 1, 2, and 3 days later respectively. It will be seen that mice show some refractoriness as early as 24 hours after the M.H.V.-terramycin treatment.

It appeared to us that the refractory state of the mice could possibly be induced by M.H.V. which had been rendered incapable of multiplying by the action of the terramycin. This possibility we showed to be improbable by the type of experiment (table II) in which groups of mice were challenged 8 days after receiving terramycin and falling tenfold dilutions of M.H.V. Since high dilutions of M.H.V. given on the same day as terramycin induced the refractory state, it seemed unlikely to be due to a non-multiplying agent. The rapidity of induction of the resistance suggested that we might be dealing with interference rather than with true immunity, and we therefore wondered whether an avirulent terramycin-resistant variant of M.H.V. could be interfering with the development of the fatal infection.

To test this possibility we killed, on the 5th day, mice which had received M.H.V. and terramycin, and passed liver-spleen extract to other mice, with a view to challenging them later. The unchallenged controls as well as the challenged mice developed hepatitis. When, however, we repeated the experiment giving five daily doses of terramycin, we harvested an extract which was not lethal to mice, yet which made them refractory to challenge 3 or 5 days later. We maintained the avirulent agent for five passes by treating daily with terramycin the pass mice injected with virus. This type of experiment was repeated a number of times with satisfactory results. In one such experiment in which five serial passages were carried out, the mice received a dose of 1 mg. terramycin on the third and again on the fourth day after injection with virus. At each passage another group of mice received virus but no terramycin; these mice were challenged as shown in table III. It will be seen that the mice which received extract and no terramycin at each pass and were challenged 3 and 5 days later mostly survived, whereas nearly all the controls of the challenge virus died. In some experiments the challenge controls received liver-spleen extract from normal V.S. mice, but such were not significantly protected against challenge. If, however, several passes of avirulent virus were made in mice untreated with terramycin, especially if these were made at 7-day intervals, virulent M.H.V. reappeared in some series. Nevertheless we had

TABLE I—PROTECTIVE EFFECT OF M.H.V. AND TERRAMYCIN AGAINST CHALLENGE WITH 1000 L.D.$_{50}$ OF VIRUS

Inoculum	Time of challenge (hours)	Mortality ratios
Terramycin	24	5/5*
	48	5/5
	72	6/6
Terramycin + 1000 L.D.$_{50}$ M.H.V.	24	6/8
	48	0/6
	72	0/4

*5/5 indicates that 5 out of 5 challenged mice died.

TABLE II—EFFECT OF TERRAMYCIN ON MOUSE-HEPATITIS VIRUS

Inoculum	Mortality ratios* at dilution				
	10^{-1}	10^{-2}	10^{-3}	10^{-4}	10^{-5}
Virus only	5/5	5/5	5/5	5/5	5/5
Virus + terramycin	0/5	0/5	0/4	0/5	0/5
Virus + terramycin challenged on 8th day by approx. 1000 L.D.$_{50}$	0/5	0/5	0/4	1/5	2/5

* Includes mice sacrificed with typical lesions.

TABLE III—RESULTS OF CHALLENGING MICE PREVIOUSLY INJECTED WITH TERRAMYCIN-RESISTANT VIRUS

No. of pass	Days between injection and challenge	Dilution of virus used to immunise	Mortality ratio	
			Challenged group	Control group
2	3	10^{0}	3/5	6/6
3	5	10^{0}	0/6	5/6*
4	5	10^{-3}	0/5	5/6

* 5/6 = death from hepatitis in 5 out of 6 mice.

passed an avirulent but immunising agent sufficiently often to feel moderately confident that our working hypothesis was correct in that we had a transmissible terramycin-resistant agent distinct from M.H.V. Later we found that an agent in no way distinguishable from this could be obtained much more conveniently by allowing M.H.V. tissue extracts to stand on the laboratory bench overnight at about 20°C. This we called "S." because of its relative stability on standing.

Discovery of "L.," the Labile Component of M.H.V.

One doubt remained: could the transmissible immunising agent consist after all of M.H.V. kept down by terramycin to a low level at which it could not produce disease? To test this possibility groups of mice were infected with virulent M.H.V. at dilutions higher than the lethal dilution and challenged several days later to see if they had become refractory; an example of such an experiment is shown in table IV. It was found that mice treated in this way not only did not become refractory but, when challenged several days later, died more quickly than controls. Thus, in table V, the challenged controls died in a mean of 5·9 days as against 4·4 days for the mice which received the double inoculation. The difference between these averages in this single experiment is statistically significant, owing to the small variability in the times of individual deaths. Amongst other experiments carried out when seeking an explanation of this finding, we injected mice which had received a sublethal dose of M.H.V., with S., the avirulent agent obtained from terramycin-treated mice. These mice died of M.H.V. hepatitis whereas the controls did not. Such an experiment is illustrated in table V. Experiments of this kind were successful whether the S. component was mixed with sublethal dilutions of M.H.V. or injected as long as 5 days later.

The high-titred labile component (L.) was obtained from M.H.V. without difficulty by passing at 3-day intervals M.H.V. diluted 10^{-5}, 10^{-6}, 10^{-7}, and 10^{-8} and finding the highest dilution producing hepatitis when mixed with the S. component; we hoped by this limiting dilution method to identify a preparation free from S. L. so obtained was propagated by passing it alternately undiluted and diluted 10^{-7} at 3-day and 4-day intervals.

Passage in Mice of S. and L. and their Recombination

Many of our earlier experiments gave inconclusive results because we could not guarantee that supposedly pure L. and S. would not kill a few mice. Thus in one such experiment 1 of 25 mice used in six serial passes of "L." died with hepatitis, and 5 of 30 mice died in the course of six serial passes of S.; by contrast, 27 of 27 died when L. and S. were recombined. More recently the method of passing L. twice weekly and diluting 1 : 10^{7} at every other pass has given us L. preparations which have killed none out of 46 mice in the course of twenty-two passes. If, however, such L. is passed at 7-day intervals in V.S. mice without any diluting, hepatitis due to M.H.V. has appeared, for by such a method S. can be picked up from V.S. mice and the virulent combination reconstituted. Similarly by a limiting dilution method we have now obtained from M.H.V. suspensions allowed to stand, an S. preparation which is perhaps pure as no specific deaths have occurred amongst 36 V.S. mice used in six passes. Deliberate recombination of these "pure" L. and S. lines produced fatal hepatitis in 100% of mice: this has occurred after five passes of pure S. and twenty-two passes of pure L.

TABLE IV—POTENTIATING EFFECT OF SUBLETHAL DOSES OF M.H.V. ON SUBSEQUENT CHALLENGE

Dilution of inoculum	Challenge $L.D._{50}$	Mortality ratio	Average survival-time (days)
10^{-4}	Nil	1/10	6
10^{-4}	1000 (approx.)	10/10	4·4
None	1000 (approx.)	11/11	5·9

Properties of L. and S.

L. seems harmless even to newborn mice. S., on the other hand, will produce hepatitis, often fatal, in mice up to about 1 week of age. Passage from livers of these baby mice yields only S., not the complete M.H.V.

The filterability of L. and S. is still under investigation. S. has several times been passed through a gradocol membrane of 250 mμ average pore diameter (A.P.D.); on one occasion we failed to pass it through one of A.P.D. 110 mμ. L. seems to be somewhat larger; it has passed through a membrane of 350 mμ A.P.D. but failed to pass through one of 250 mμ A.P.D. M.H.V. itself was shown to pass through a membrane of 300 mμ A.P.D. but, like L., not through ones of 250 mμ A.P.D. (Gledhill and Andrewes 1951).

TABLE V—EFFECT OF S. UPON MICE PREVIOUSLY INFECTED WITH SMALL DOSES OF M.H.V.

1st intraperitoneal inoculation	2nd intraperitoneal inoculation 72 hr. later	Mortality ratio	Average survival-time (days) of mice which died
M.H.V. 10^{-6}	..	2/16	8·5
"	S	0/3	
M.H.V. 10^{-4}	S	6/6	5·0

It is possible to measure the $L.D._{50}$ of extracts of L. for a constant dose of S. and, likewise, the $L.D._{50}$ of S. for a constant dose of L. This has been done on several occasions for L. (S. constant) and gave values of between 10^{-7} and 10^{-9} ml. as against 10^{-4} to 10^{-6} ml. for M.H.V. itself. The $L.D._{50}$ of S. (L. constant) gave values of 10^{-3} to 10^{-4} ml.

L. and S. are both inactivated by heating to 56°C for 30 min.; and by treatment with 20% ethyl ether overnight at +2°C.

DISCUSSION

The experiments reported above are readily reproducible: their interpretation is far from clear. It is uncertain whether L. and S. are two unrelated viruses or whether they are alternative phases of one virus. A third, much less likely, possibility is that M.H.V. is a real entity, not merely a mixture of L. and S., and that L. and S. are variants of it. Our discovery that two components could be obtained from M.H.V. depended upon several fortunate chances, particularly the susceptibility of L. but not S. to terramycin. The demonstration that a virus can be so split may lead others to examine other virus infections from this point of view; if the possibility is not in mind, such a complex ætiology might long be overlooked. Plant pathologists are familiar with the idea that two relatively innocuous viruses may, when they co-exist in a plant, produce a serious disease: the infection of tomatoes by a combination of potato virus X and tobacco mosaic is an example (Bawden 1946).

It seems probable that L. is carried in the blood and tissues of a majority of P. but not V.S. mice. S. is probably

carried by both breeds, but if it were present in only a small proportion of V.S. mice one could readily account for the varying number of blind passes necessary to produce hepatitis in the serial passage technique we have used (P.→V.S.→V.S. . . . &c.). Such a state of affairs would account for our failure to keep L. permanently pure and avirulent when passed in V.S. mice, except by the help of special precautions.

The production of hepatitis by inoculating blood of normal mice into other normal mice is an occurrence having obvious possible analogies with homologous-serum jaundice in man. M.H.V. is much more labile than the human virus, but the S. component is fairly stable, though even it does not resist 20% ether nor exposure to 56°C for half an hour: it is also a small virus, though its size has not yet been determined accurately.

The mechanism whereby these two agents act synergically to produce a fatal disease is still under investigation.

SUMMARY

Further work is reported concerning a virus causing fatal hepatitis in mice. This was obtained by taking blood or viscera or normal mice of one strain (P.) and making serial intraperitoneal passages in young mice of another strain (V.S.). The hepatitis could be prevented by a single dose of terramycin or aureomycin.

The mouse-hepatitis virus (M.H.V.) has now been resolved into two components, one relatively stable (S.) and one more labile (L.). S. is obtained from mice inoculated with M.H.V. and treated by terramycin, to which it is resistant; or by allowing suspensions of M.H.V. to stand at about 20°C for 24 hours; the L. then dies out. L. is present in M.H.V. suspensions to higher titre than S. and is obtained by passage at limiting dilutions. Neither L. nor S. when given separately to recently weaned V.S. mice produces any evident disease; when given together they cause fatal hepatitis. L. and S. are both transmissible in series and are presumably viruses—either separate entities or, less probably, phases or variants of one virus. S. is apparently smaller than L.

REFERENCES

Bawden, F. C. (1946) *J. R. Soc. Arts*, **94**, 136.
Gledhill, A. W., Andrewes, C. H. (1951) *Brit. J. exp. Path.* **32**, 559.
Webster, L. T. (1937) *J. exp. Med.* **65**, 261.

THE DIAGNOSTIC VALUE OF ESTIMATIONS OF PROTEIN-BOUND IODINE IN SERUM

R. R. DE MOWBRAY
B.M. Oxfd, M.R.C.P.
REGISTRAR TO THE BASAL METABOLIC RATE AND ENDOCRINE DEPARTMENT

A. TICKNER
M.B., B.Sc. Lond.
JUNIOR LECTURER, DEPARTMENT OF CHEMICAL PATHOLOGY

GUY'S HOSPITAL, LONDON

THE blood-iodine level was estimated as long ago as 1900, by Gley and Bourcet, and numerous techniques have been introduced for its measurement since then; but it is only within the past ten years that reliable methods have become available for clinical purposes. Practically all the work in this field has been done in America, and very little has been written about it in this country. The subject is fully reviewed by Rapport and Curtis (1950).

NATURE OF BLOOD-IODINE

The blood-iodine is predominantly bound to the plasma-proteins: 75% of it is present in the albumin fraction; some of it is found in the α-globulin fraction, and a smaller amount in the β-globulin fraction; but the γ-globulins play no part in binding iodine. The inorganic iodine content of the blood is usually negligible, but it varies considerably with the iodine content of the diet and is greatly increased by the administration of iodides (Bassett et al. 1941, Riggs et al. 1942, Taurog and Chaikoff 1948).

There is considerable evidence that the amount of protein-bound iodine in the serum is an index of the amount of circulating thyroxine, as shown by its chemical behaviour and by experiments with radioactive iodine (Chaikoff et al. 1947, Taurog and Chaikoff 1948).

MATERIAL AND METHODS

The series reported here consists of estimations of the level of protein-bound iodine in the serum of 30 normal people and 375 hospital patients. In 317 cases the basal metabolic rate (B.M.R.) was also estimated, and in 243 cases the serum-cholesterol level was determined.

The level of protein-bound iodine in the serum was estimated by the method of Barker (1948); 10 ml. of blood was collected at any convenient time of the day, with no particular time-relationship to meals. Barker's method is very sensitive and 0·01 μg. of iodine may be estimated relatively easily.

The apparatus was modified slightly by Mr. R. A. Adams who introduced a stoppered side-arm just below the condenser, so that sodium-sulphite solution could be introduced into the trap without disturbing the condenser. Our experience with the method agrees well with Barker's, but the following comments should be made: (1) our recoveries of iodine from thyroxine, added before digestion, were about 100% rather than 90%; we do not therefore make any correction for losses during distillation; and we believe that different stills vary slightly in efficiency; (2) The grade of sulphuric acid mentioned by Barker does not seem to be available in this country; in our experience the purity of this reagent is the most important factor in the attainment of low blank values; the most satisfactory grade that we have tried is the 'M.A.R.' grade of Messrs. Hopkins and Williams; this should be boiled with hydrochloric acid, as described by Barker, for at least two hours on the same day as the estimation is made.

The serum-cholesterol level was estimated by the method of Bloor (1916). In practically every case the levels of serum-cholesterol and protein-bound iodine were estimated on the same sample of blood.

The B.M.R. was determined by the method of Robertson (1944). A Kendrick apparatus was used. Estimations were made both on outpatients and on inpatients, and the subject rested for half an hour before each test. Two recordings of ten minutes each were made consecutively in all cases, a trial reading having been made on the preceding day in those cases in which the patient had not previously been tested. In most cases agreement between the two consecutive readings was within 5%. The B.M.R. was determined, so far as possible, on the same day as blood was taken for the estimations of cholesterol and protein-bound iodine, usually within a few days, and always within a week.

All the estimations of protein-bound iodine in the serum that were made in the past two years have been recorded here, except that we have only included those in which satisfactory duplicate readings were obtained, and that we have excluded cases of thyroid disorder in which previous treatment has prevented an adequate assessment of the thyroid state.

NORMAL RANGES

We obtained a range of 4–8 μg. per 100 ml. of serum for protein-bound iodine in 30 normal people, with a mean of 5 μg. per 100 ml. The duplicate determinations usually agreed to within 1 μg. per 100 ml., and the result was not accepted if they differed by more than this amount. Consequently the results have been expressed to the nearest microgramme, the decimal points being ignored. Most other workers have also found a normal range of about 4–8 μg. per 100 ml.

Though we found a range of 4–8 μg. per 100 ml. in normal healthy people, some patients who were

clinically euthyroid showed levels as low as 3 μg. per 100 ml., and a few gave figures even lower than this. The lower level is therefore indefinite, and only figures of less than 3 μg. per 100 ml. can be regarded as abnormally low. On the other hand, the upper limit of normal in our series was remarkably well defined; any figure exceeding 8 μg. per 100 ml. could be regarded as significantly high.

The normal range of serum-cholesterol levels determined in our laboratories is 150–350 mg. per 100 ml. (Foote and Merivale 1949), a wider range than is usually recognised.

Our normal range for the B.M.R. is from 0 to −20%. The reason for this difference from the usually accepted range (from +10% to −10%) is probably that the Du Bois standards of height-weight-surface area and oxygen consumption per unit of surface area are calculated from American and not British people.

LIMITATIONS AND SOURCES OF ERROR IN DETERMINATION OF PROTEIN-BOUND IODINE IN SERUM

Administration of Iodine Compounds

The level of protein-bound iodine in the serum may be increased by iodine from various extraneous sources. If meticulous care is taken to exclude traces of iodine from the apparatus, the only important source of confusion is the previous administration of iodine to the patient. Small amounts of inorganic iodine should be eliminated from the serum by repeated and careful washings during the estimation. If large amounts of inorganic iodide are administered, iodine compounds are formed which are apparently adsorbed on to the serum-proteins and increase the level of protein-bound iodine. This increase may persist for a week after the iodine therapy has been discontinued, and outlasts the rise in inorganic-iodide level in the serum; the thyroxine level is, however, not increased (Bassett et al. 1941, Salter 1947, Danowski and Greenman 1949, Danowski et al. 1950a and b, Starr et al. 1950).

The administration of organic iodine compounds is particularly likely to increase the amount of protein-bound iodine in the serum. This effect may persist for as long as three months or even a year after a cholecystogram (Riggs 1947, Starr et al. 1950), and for as long as five years, and even perhaps permanently, after the intrathecal injection of 'Lipiodol' (Hallman et al. 1951). The level of protein-bound iodine in the serum may also be raised after bronchography or salpingography, or after the injection of sinus tracts with lipiodol. Pyelography may have similar effects, but they are much more short-lived, since the iodine compound is rapidly excreted in the urine and disappears within 1–4 weeks (Riggs 1947, Starr et al. 1950, Hallman et al. 1951).

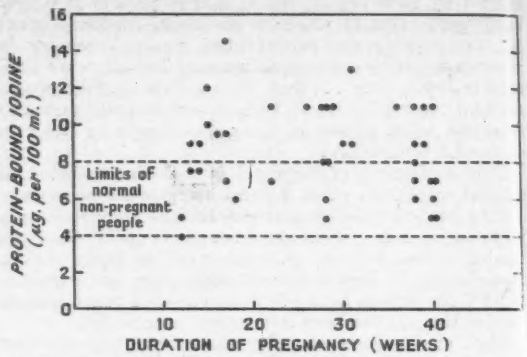


Fig. 1—Levels of protein-bound iodine in serum of 41 normal pregnant women.

Pregnancy

The protein-bound iodine in the serum was estimated in 41 healthy women with normal pregnancies. 22 (54%) of these showed levels exceeding 8 μg. per 100 ml. between the thirteenth and last weeks of pregnancy. The range of values was 4–20 (mean 8·8) μg. per 100 ml. (fig. 1). Similar findings have been made by other workers who have found that the level may be raised as early as six weeks after conception (Man et al. 1951). It is interesting, in this connection, that the B.M.R. is also raised in normal pregnancy.

RESULTS

The values obtained for protein-bound iodine and cholesterol in the serum and for the B.M.R. in various disorders are recorded in the accompanying table and fig. 2.

Hyperthyroidism

The level of protein-bound iodine in the serum was raised in only 61% of the cases, whereas the B.M.R. was raised in all the cases. The serum-cholesterol level was reduced in only 11% of the cases. Each case was carefully assessed on clinical grounds (resting pulse-rate; tem-

COMPARISON OF LEVELS OF PROTEIN-BOUND IODINE AND CHOLESTEROL IN SERUM AND B.M.R. IN VARIOUS CONDITIONS

Clinical diagnosis	Protein-bound iodine (μg. per 100 ml.)						Basal metabolic rate (%)						Serum-cholesterol (mg. per 100 ml.)						Agreement with clinical diagnosis (%)		
	No. of cases tested	(No. of cases)			Range	Mean	No. of cases tested	(No. of cases)			Range	Mean	No. of cases tested	(No. of cases)			Range	Mean	Protein-bound iodine	B.M.R.	Cholesterol
		∧ 8	3–8	∨ 3				∧ 0	From 0 to −20	∨ −20				∨ 150	150–350	∧ 350					
Non-toxic goitre	59	1	53	5	1–11	5·4	43	2	39	2	−24 to +6	−9	37	1	31	5	140–422	266	81	90	86
Hyperthyroidism	64	39	25	0	4–20	10·2	53	53	0	0	+5 to +65	+23	54	6	48	0	109–328	202	61	100	11
Borderline hyperthyroidism	28	12	14	2	2–20	7·4	23	15	8	0	−17 to +37	+5	17	1	15	1	120–400	235	..	..	..
Myxœdema	9	0	1	8	0–3	1·2	9	0	0	10	−24 to −47	−31	9	0	4	5	160–530	391	89	100	56
Doubtful hypothyroidism	9	0	8	1	2–6	4·1	8	1	3	4	−26 to +8	−17	9	0	7	2	231–490	317	..	..	..
Panhypopituitarism	3	0	0	3	2	2	3	0	0	3	−31 to −45	−36	3	0	1	2	315–420	384	..	..	..
Anxiety state	13	2	9	2	1–18	5·3	5	0	5	0	−10 to −19	−14	6	0	6	0	214–275	211	69	100	100
Acromegaly	6	1	5	0	3–22	7·2	6	3	2	1	−21 to +11	−2	5	0	5	0	200–400	271	..	..	..
Obesity	51	1	48	2	2–11	5·1	24	0	17	7	zero to −34	−16	47	1	42	4	114–450	241	..	..	..

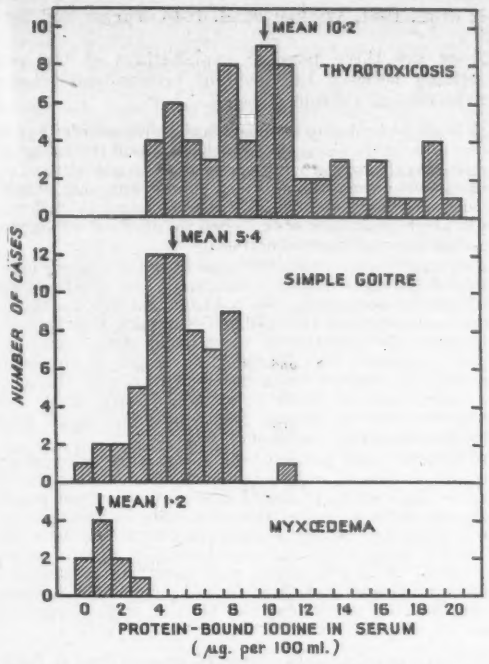


Fig. 2—Distribution of levels of protein-bound iodine in serum in various thyroid disorders.

perature and moisture of the skin ; presence or absence of tremor, exophthalmos, or lid retraction ; and response to treatment with iodine, thiouracil, or thyroidectomy) and, in surgical cases, by the histology of the thyroid gland. We have included in this group only those cases in which a diagnosis of the hyperthyroidism was established beyond doubt on the basis of these criteria.

In 2 cases with normal initial levels of protein-bound iodine the levels were found to be raised some weeks later, even though both patients had been treated with thiouracil during that period. It is likely that other cases would have shown similar fluctuations if repeated estimations had been made. Random estimations during anti-thyroid treatment gave varied results (fig. 3).

Non-toxic Goitre

The amount of protein-bound iodine in the serum was normal in 81% of the cases, the B.M.R. normal in 90% of the cases, and the serum-cholesterol level normal in 86% of the cases. Apart from the single raised value of protein-bound iodine included in the table, 2 other cases showed raised values attributable to the recent administration of iodine. The finding of levels below 3 μg. per 100 ml. in 8% of the cases is difficult to explain ; none of these cases showed any other evidence of hypothyroidism.

Borderline Hypothyroidism

In many of the cases the amount of protein-bound iodine in the serum and the B.M.R. were not in agreement. The B.M.R. was estimated in 11 of the 12 cases with increased amounts of protein-bound iodine, and in only 6 of these was it increased ; in only 5 of the 15 cases with a raised B.M.R. was the amount of protein-bound iodine in the serum increased. Since the B.M.R. was increased in all the cases of undoubted hyperthyroidism and was normal in 90% of the cases of non-toxic goitre, and since the amount of protein-bound iodine in the serum was increased in only 61% of the cases of proved hyperthyroidism and was normal in only 81% of the cases of non-toxic goitre, we place more reliance on the B.M.R. in the diagnosis of borderline cases.

Myxœdema

The level of protein-bound iodine in the serum and the B.M.R. was compatible with the diagnosis in all the cases, except one in which the level of protein-bound iodine was in the low normal range (3 μg. per 100 ml.). In another case two separate readings of 0 and 3 μg. per 100 ml. were obtained before treatment was started. The serum-cholesterol level was raised in only 56% of the cases. In another case, not included in the table, the amount of protein-bound iodine in the serum was 15 μg. per 100 ml. This patient had received several courses of thyroid extract in the past, but had had to discontinue the treatment each time after a week because she could not tolerate it. She had received no thyroid treatment since a year before the estimation was made ; at that time she had been given crystalline thyroxine 0·2 mg. daily for eight weeks.

Panhypopituitarism

The level of protein-bound iodine in the serum was reduced in each of 3 classical cases of post-partum Simmonds's disease with clinical signs of hypothyroidism, in spite of the fact that 1 of them had been receiving gr. 1 of thyroid extract daily for eight years.

Acromegaly

The levels of protein-bound iodine in the serum were essentially normal in 5 of the 6 cases in spite of a slightly raised B.M.R. in 3 cases. In 1 case the level fluctuated in a most remarkable manner between 22 and 3 μg. per 100 ml. within a few weeks ; the B.M.R. ranged between +11% and −4% during this period.

Other Endocrine Disorders

The level of protein-bound iodine in the serum was grossly reduced in 2 out of 12 cases of pituitary infantilism, but was normal in 2 cases of Cushing's syndrome, 1 case of Addison's disease, 2 cases of eunuchoidism, and 2 cases of ovarian agenesis.

Miscellaneous Disorders

The level of protein-bound iodine in the serum was reduced in 9 out of 50 patients with various skin disorders, including alopecia and keratosis pilaris. One of the

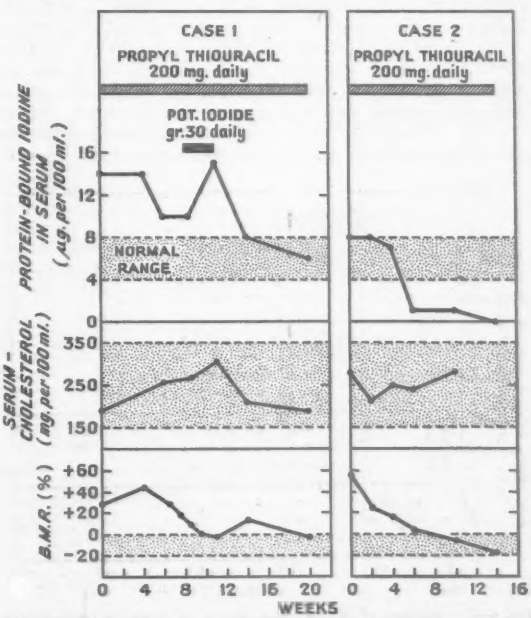


Fig. 3—B.M.R. and levels of protein-bound iodine and of cholesterol in serum in two cases of hyperthyroidism under treatment.

cases of keratosis pilaris was associated with myxœdema, but the other cases showed no evidence of hypothyroidism. Low values for protein-bound iodine were also obtained in 2 out of 52 cases of obesity and in 1 out of 5 cases of dystrophia myotonica. Raised levels were found in 6 other patients, 2 of whom had recently been treated with thyroid extract.

DISCUSSION

The table shows that the level of protein-bound iodine in the serum agrees with the clinical diagnosis less closely than does the B.M.R.: the over-all agreement is only 77% for protein-bound iodine, compared with 97% for the B.M.R. There is a considerable overlap between the values of protein-bound iodine obtained in euthyroid people and those obtained in patients with disorders of thyroid function. Though only about two-thirds of the patients with hyperthyroidism showed raised levels of protein-bound iodine, such raised levels as did occur were practically confined to hyperthyroidism or to pregnancy, or to patients to whom iodine-containing compounds had recently been administered. On the other hand, the level of protein-bound iodine was consistently subnormal in hypothyroidism and panhypopituitarism, though low values were also obtained in some euthyroid people with simple goitres and various non-endocrine disorders. This overlap severely limits the value of the estimation in the diagnosis of borderline cases; in our experience the B.M.R. is more helpful for this purpose.

Our findings therefore disagree with those of most American workers. Salter et al. (1941) found that the level of protein-bound iodine agreed with the clinical diagnosis in 98% of cases, whereas the B.M.R. agreed in only 71%. Riggs (1947) found the level of protein-bound iodine to be compatible with the clinical diagnosis in 85–89% of 325 cases. Winkler et al. (1946) and Salter et al. (1941) found it raised in 95% of cases of hyperthyroidism, and Hallman et al. (1951) in 100%. Starr et al. (1950) found it raised in 94% of cases of hyperthyroidism, but in a few cases they obtained values within the low normal range; in other conditions their findings were similar to ours, and, like us, they found some subnormal values in conditions other than hypothyroidism—e.g., diabetes mellitus, obesity, and heart-failure—in various psychoses, and in some elderly people.

We have found a rough correlation between the amount of protein-bound iodine in the serum and the B.M.R. at various levels of thyroid function, but when one set of values is plotted against the other the scatter is diffuse (fig. 4). Other workers have claimed a closer correlation than this (Salter et al. 1941, Bassett et al. 1941, Lowenstein et al. 1944, Winkler et al. 1946, Tucker and Keys 1951).

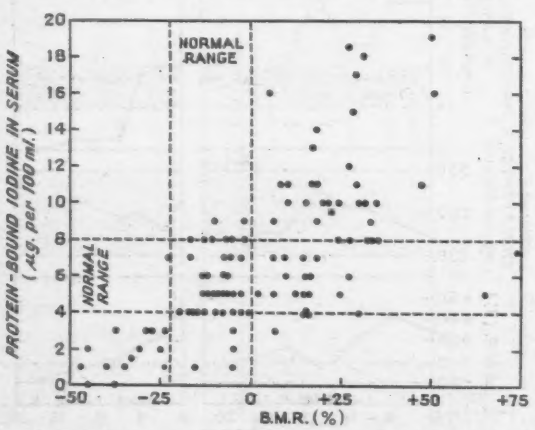


Fig. 4—Correlation of B.M.R. and levels of protein-bound iodine in serum in cases of hyperthyroidism, non-toxic goitre, and hypothyroidism.

There are three possible explanations of the poor correlation between the level of protein-bound iodine and the clinical thyroid state:

(1) It might be due to technical faults. We guarded against this by making duplicate determinations in all the cases, and by repeating the estimation if agreement was not within 1 μg. Moreover our normal range agreed closely with that of other workers, and very few raised levels were found in euthyroid people which could not be explained by previous administration of iodine or of thyroid extract.

(2) We have shown that the level of protein-bound iodine fluctuated in 2 cases of hyperthyroidism, 1 case of myxœdema, and 1 case of acromegaly. It is likely that this fluctuation occurs commonly, and that a single estimation may therefore not give a true reflection of the thyroid state. Since the metabolic response lags behind the changes in circulating thyroxine, fluctuations could occur without any change in the clinical picture. Starr et al. (1950) have shown that fluctuations occur in normal people as well, though these do not extend outside the normal range.

(3) Perhaps some patients will develop hyperthyroidism or hypothyroidism in response to levels of circulating thryoid hormone which would be regarded as normal in most people. Some cases of simple goitre have shown low levels of protein-bound iodine, and in such cases a rise of the level to within the normal range might well be followed by signs of hyperthyroidism. It is well known that endocrine function and dysfunction depend not only on the amount of hormone secreted but also on the response of the "target" organ or tissue.

We have not found the level of protein-bound iodine in the serum to be a reliable guide to treatment. The administration of iodine to patients with hyperthyroidism has tended to raise the level of protein-bound iodine still higher. Under treatment with thiouracil the level has in some cases fallen in parallel with the response of the clinical condition and the B.M.R., though in other cases it has preceded it. In 2 cases the level has actually risen during treatment. The level of protein-bound iodine may actually fall below the normal range without any clinical evidence of hypothyroidism (fig. 3). These findings are again at variance with those of other workers. Man et al. (1942) and Winkler et al. (1946) found that the administration of iodine to patients with hyperthyroidism reduced the level of protein-bound iodine, sometimes to within the normal range, thus reflecting the clinical response. Most workers have found that the fall in the level of protein-bound iodine during thiouracil therapy precedes the clinical response and fall in B.M.R. by some days or even weeks (Lowenstein et al. 1945, Engstrom et al. 1950, Hallman et al. 1951), and Engstrom et al. (1950) regarded a subnormal value of protein-bound iodine, at any stage, as an indication of over-treatment.

In the treatment of myxœdema we have found, as did Robertson and Kirkpatrick (1952), that the B.M.R. is a more accurate guide than the level of protein-bound iodine. The administration of thyroid extract may in itself increase the level of protein-bound iodine in patients who show no signs of over-treatment. A similar increase may follow the administration of thyroid extract to euthyroid people.

Perhaps the chief value of estimating the protein-bound iodine in the serum is in the diagnosis of thyroid disorders where determination of the B.M.R. is impracticable—e.g., in infants and young children, in elderly persons, in cardiac failure and chest disease, and in neurological and mental disease. It may also be helpful in distinguishing thyroid disorders from other conditions with a raised or lowered B.M.R.

There are two disadvantages of the estimation: (1) the technical difficulties are considerable, and it is essential that duplicate determinations should be made by two different people who are practising the technique constantly; and (2) the result may be vitiated by previous

administration of iodine-containing compounds. Provided, however, that the latter can be excluded, and that the patient is not pregnant, a raised level of protein-bound iodine practically always indicates hyperthyroidism, though a normal level by no means excludes it. A low level does not necessarily indicate hypothyroidism, but a normal level virtually excludes it.

One could not do better than to sum up in the words of Means (1948):

"Both the B.M.R. and blood-iodine tell something of thyroid function, but different things. The B.M.R. is an index of the total effect of the thyroid hormone on its end-organs. Its level would depend not only on the amount of hormone discharged, but also on the sensitivity of the end-organs. The protein-bound iodine of the blood merely represents the level of hormone in the blood, which is dependent on the rate of delivery of hormone to, and removal from, the blood. Collection of radioactive iodine is an index of the thyroid's hunger for iodine, which is probably related to its degree of stimulation. Therefore it is not a question of which of these measuring sticks is best. All are of value; the more of them which are used, the more understanding is to be derived from them."

SUMMARY

The levels of protein-bound iodine in the serum were estimated in 30 normal people and 475 hospital patients.

The normal range was 4–8 μg. per 100 ml.

Only 61% of the patients with proved hyperthyroidism showed levels above 8 μg. per 100 ml. With few exceptions, readings of more than 8 μg. per 100 ml. were confined to hyperthyroidism, pregnancy, or cases in which iodine had previously been administered.

The level was consistently reduced in myxœdema and panhypopituitarism, but some low values were obtained where there was no clinical evidence of hypothyroidism.

The B.M.R. was of more value in the diagnosis of thyroid disorders and in assessing the response to treatment.

The serum-cholesterol level was of little value in the diagnosis of hyperthyroidism; it was helpful, but less reliable than the level of protein-bound iodine, in the diagnosis of hypothyroidism.

It is technically difficult to estimate the level of protein-bound iodine in the serum, and the results are liable to be vitiated by previous administration of iodine compounds in any form.

Apparently the value may fluctuate between normal and abnormal levels.

The level of protein-bound iodine in the serum is merely an index of the amount of circulating thyroxine. The response to a given level of hormone apparently varies in different people.

The chief use of the estimation of the level of protein-bound iodine in the serum is in cases in which measurement of the B.M.R. is impracticable or subject to error.

In itself it is not a reliable index of thyroid function but, if used in conjunction with other tests and with sound clinical judgment, it may be of considerable value.

We are grateful to Dr. P. M. F. Bishop and Prof. R H. S. Thompson, in whose departments this work was done, for valuable advice; Mr. R. A. Adams for technical assistance in the estimations of protein-bound iodine; and Dr. W. H. H. Merivale and his technicians in the department of clinical pathology for the cholesterol estimations and for help with the B.M.R. estimations.

REFERENCES

Barker, S. B. (1948) *J. biol. Chem.* **173**, 715.
Bassett, A. M., Coons, A. H., Salter, W. T. (1941) *Amer. J. med. Sci.* **202**, 516.
Bloor, W. R. (1916) *J. biol. Chem.* **24**, 227.
Chaikoff, I. L., Taurog, A., Reinhardt, W. O. (1947) *Endocrinology*, **40**, 47.
Danowski, T. S., Greenman, J. H. (1949) *Fed. Proc.* **8**, 31; *Trans. Amer. Goiter Ass.*, p. 154.
— Johnston, S. Y., Greenman, J. H. (1950a) *J. clin. Endocrinol.* **10**, 519.
— Mateer, F., Weigand, F. H., Peters, J. H., Greenman, J. H. (1950b) *Ibid*, p. 532.
Engstrom, W. W., Kydd, D. M., Man, E. B., Peters, J. P. (1950) *Ibid*, p. 1251.

References continued at foot of next column

SOME EFFECTS OF LONG-CONTINUED CORTISONE THERAPY IN RHEUMATOID ARTHRITIS

H. F. WEST
M.D. Lond., M.R.C.P., D.T.M.
CONSULTING PHYSICIAN FOR RHEUMATIC DISEASES

G. R. NEWNS
M.B. Birm., M.R.C.P.
SENIOR REGISTRAR, RHEUMATISM UNIT
UNITED SHEFFIELD HOSPITALS

From the Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases

OF six patients who began continuous cortisone-acetate therapy for rheumatoid arthritis twenty-one months ago, three are well, one is in a worse state than when she started treatment, and two are dead. We report here some revealing observations made on these patients. They do not necessarily detract from the value of cortisone acetate as a therapeutic agent.

THE SIX PATIENTS

The first three are females, aged 16, 22, and 36. They have received and still receive 50–75 mg. of cortisone acetate daily. The first remains well and fully active but has more joints affected now than at the beginning of treatment. The second maintains improvement but is still very thin and has little vitality. The third has so far responded very nearly perfectly. In all three cases the erythrocyte-sedimentation rates and hæmoglobin concentrations approached normal in the early weeks of treatment but have remained respectively above and below normal ever since. The menstrual function and feminine attributes have become and remained normal, suggesting that cortisone acetate, in the doses used, does not suppress adrenal functions which it cannot replace. This may only apply to women in the childbearing years. As so few have been treated in this way for $1^1/_2$ years this tentative conclusion may prove incorrect.

The fourth patient is a woman of 49 who is three years past the menopause.

In the early weeks of treatment an average dose of 50 mg. of cortisone acetate a day brought about really amazing improvement; but, as the months went by, larger doses became necessary. By the ninth month 150 mg. a day was barely sufficient to prevent the return of pain and swelling to all her peripheral joints.

On this high dose abnormal deposits of fat developed, and she became hypertensive (highest recorded blood-pressure 210/120 mm. Hg). Seven months on a lower dose averaging 75 mg. a day has led to the loss of much abnormal fat and the return of blood-pressure to normal, but the rheumatoid disease has increased, generalised stiffness and muscle weakness

DR. DE MOWBRAY, DR. TICKNER: REFERENCES—*continued*

Foote, J. B., Merivale, W. H. H. (1949) *Guy's Hosp. Rep.* **98**, 202.
Gley, E., Bourcet, P. (1900) *C. R. Acad. Sci., Paris*, **130**, 1721.
Hallman, B. L., Bondy, P. K., Hagewood, M. A. (1951) *Arch. intern. Med.* **87**, 817.
Lowenstein, B. E., Bruger, M., Hinton, J. W., Lough, W. G. (1945) *J. clin. Endocrinol.* **5**, 181.
— — — Member, S. (1944) *Ibid*, **4**, 268.
Man, E. B., Heinemann, M., Johnson, C. E., Leary, D. C., Peters, J. P. (1951) *J. clin. Invest.* **30**, 137.
— Smirnow, A. E., Gildea, E. F., Peters, J. P. (1942) *Ibid*, **21**, 773.
Means, J. H. (1948) *West. J. Surg.* **56**, 65.
Rapport, R. L., Curtis, G. M. (1950) *J. clin. Endocrinol.* **10**, 735.
Riggs, D. S. (1947) *Trans. Amer. Goiter Ass.* p. 137.
— Lavietes, P. H., Man, E. B. (1942) *J. biol. Chem.* **143**, 363.
Robertson, J. D. (1944) *Brit. med. J.* i, 617.
— Kirkpatrick, H. F. W. (1952) *Ibid*, i, 624.
Salter, W. T. (1947) *West. J. Surg.* **55**, 15.
— Bassett, A. M., Sappington, T. S. (1941) *Amer. J. med. Sci.* **202**, 527.
Starr, P., Petit, D. W., Chancy, A. L., Rollman, H., Aiken, J. B., Jamieson, B., Kling, I. (1950) *J. clin. Endocrinol.* **10**, 1237.
Taurog, A., Chaikoff, I. L. (1948) *J. biol. Chem.* **176**, 639.
Tucker, R. G., Keys, A. (1951) *J. clin. Invest.* **30**, 869.
Winkler, A. W., Riggs, D. S., Thompson, K. W., Man E. B. (1946) *Ibid*, **25**, 404.

are pronounced, her knees are more painful and eroded, and her wrists and hands are constantly swollen and hot. Complications have included hæmorrhage from a duodenal ulcer necessitating blood-transfusion (fourth month), the appearance of severe hot flushes (controlled by œstrogen therapy), and at one stage the cortisone-withdrawal phenomenon—painful swollen joints that are eased by rest and made worse by use (rheumatoid symptoms in reverse). An unusual complication, associated with moon-face, has been the floating up of the lower denture.

This kind of response to high doses has been noted by some American physicians in postmenopausal women. In the present state of our knowledge it would be wise to avoid, for rheumatoid patients after the menopause, doses in excess of 75 mg. a day for more than a month. When worth-while control of the disease cannot be achieved with this restricted dosage, it would be best, theoretically, to change over to adrenocorticotropic hormone (A.C.T.H.) before tailing off the treatment. Such a change-over could not be completed for this patient, because she developed gross urticarial reactions to the injections. When A.C.T.H. is available free from carrier protein, this type of reaction may cease to occur.

The pathology of cortisone-withdrawal symptoms, other than those of adrenal insufficiency, has not yet been described. Perhaps some tissues become adapted to the changed environment caused by the prolonged administration of cortisone acetate and, as a consequence, manifest a new disorder when the hormone is withdrawn.

The fifth patient was a man aged 29.

His illness had begun three years previously as pericarditis and acute rheumatism, but this gradually changed to rheumatoid disease. His large joints were damaged, his feet deformed, and his hands practically useless. Six months before cortisone-acetate therapy began, a liver biopsy revealed no sign of amyloid disease.

After three months' therapy he was unwittingly given for three weeks an inactive preparation of A.C.T.H. During this time he became ill, jaundice appeared for a few days, and his liver enlarged rapidly. On the resumption of cortisone-acetate therapy he soon recovered, but his liver did not decrease in size appreciably. In the following nine months he received an average daily dose of 75 mg. At the end of a year's treatment he felt well and his rheumatoid disease was only mildly active, but his liver was enormous and he had little energy. His serum-protein levels were normal. Blood-counts showed leucocytes 20,000–30,000 per c.mm. (polymorphs 85%), hæmoglobin 12 g. per 100 ml.; and his bone-marrow showed an indeterminate picture. In the Congo-red test 99% of the dye was absorbed.

Shortly after this time he became ill suddenly. His blood-pressure fell from about 180/95 to about 80/40 mm. Hg, and he had transient abdominal pain, fever, and tachycardia. On the first day of this terminal illness his blood-electrolyte levels were normal. The dose of cortisone acetate was raised to 100 mg.; blood and, later, glucose saline solution were transfused and terramycin was given. His blood-pressure did not recover, and he died, with a falling heart-rate, on the fourth day, having passed during the four days only some 100 ml. of urine.

The liver weighed 6470 g. and about 95% of it was amyloid substance. The adrenal glands were replaced by amyloid substance save for a narrow rind of zona-glomerulosa cells. The spleen was moderately involved, but the kidneys only very slightly. Sections of the intestine, lung, heart, tongue, brain, thyroid, pituitary, and synovial membrane showed no amyloid deposit.

Many instances of amyloid disease associated with severe rheumatoid arthritis have been described; but as a gross manifestation it is rare. In the extensive literature of amyloid disease we have not found an instance of such an enormous deposition in the liver developing in so short a time. At least it may be said that in this case cortisone acetate did not retard the development of amyloid disease.

Some mice when fed, or given injections of, sodium caseinate develop amyloid disease (Smetana 1925). Our patient received calcium caseinate (' Casilan ') daily for nine months. His intestines were not involved, whereas those of the mice were. Unlike man (Gallagher et al. 1951) mice excrete steroids into the intestinal tract (Dobriner 1952). This type of experimental amyloid disease is hastened by cortisone therapy, whereas ascorbic acid has the reverse effect, for in the guineapig a state of scurvy due to ascorbic-acid depletion leads to amyloid deposition (*Lancet* 1951). Our patient received 150 mg. of ascorbic acid daily throughout the cortisone-acetate therapy. One must remember, of course, that amyloid disease is not a definable entity. The name is applied to various states in which accumulations of unknown substances with similar crude staining properties are found between the formed elements of some connective tissues. In the more common secondary varieties the defect seems to belong to the organ affected rather than to the connective tissue. The little that is known of these protein substances and their small polysaccharide moieties suggests that they differ in various diseases and from species to species (Hass et al. 1943).

The terminal event for this patient did not resemble an addisonian crisis, nor was there any evidence of septicæmia. The abdominal pain may have been caused by a small peritoneal hæmorrhage which was found at necropsy. Patients with advanced amyloid disease do not usually die in this way. One is forced to relate his death, and the mode of his dying, in some way to cortisone-acetate therapy.

The sixth patient, a man of 48, had had rheumatoid arthritis for eleven years.

When treatment with cortisone acetate began he was "at the end of his tether." During twelve months' treatment he gained much benefit and was able to keep at work. After the first six months he developed, for the first time, symptoms of a duodenal ulcer. After a further six months the ulcer bled profusely. He responded normally to treatment but stopped taking cortisone acetate twenty-five days after the hæmorrhage. For the preceding six months the dose had been 25 mg. twice daily by mouth. On the thirtieth day, without premonitory symptoms of adrenal insufficiency, he fainted, recovered consciousness for a minute, vomited, and died. At necropsy the only macroscopical abnormality was the duodenal ulcer. It had been large but had healed. Microscopically the adrenal glands were normal; the thrombus in the vessel responsible for the hæmorrhage from the duodenal ulcer was organised and already partially recanalised; and the heart showed severe subendocardial and myocardial fibrosis.

The histologically normal adrenal cortex was a pleasant surprise.

Until more is known of the action of cortisone acetate and of the ætiology of peptic ulceration, it will be advisable to discontinue cortisone-acetate therapy when ulcer symptoms appear. The apparently normal clinical and histological recovery after the ulcer bled suggests that it is not essential to stop cortisone therapy abruptly in this circumstance. To lower the dose of cortisone at any crisis is, of course, unwise in theory. The question has arisen whether, in the presence of a bleeding ulcer, oral therapy should be changed to intramuscular. It was so changed in this case—for no valid reason. Our fourth patient had received only intramuscular cortisone acetate before her ulcer bled, and a year of oral therapy since has not provoked any further bleeding.

Was the fibrosis of the heart muscle sufficient to explain sudden death, or was the cessation of cortisone therapy a necessary adjunct? We do not think that the evidence justifies a conclusion but hope that this account may prompt others to relate their similar or dissimilar experience.

CONCLUSIONS

From these observations, in conjunction with those of other workers, it seems that for women in the child-bearing years, suffering from rheumatoid arthritis, cortisone acetate 50–75 mg. a day for periods up to twenty-one months does not upset normal function.

In women after the menopause 75 mg. of cortisone acetate a day should be the maximum for maintenance therapy.

The administration of cortisone acetate and a high-protein diet in the presence of amyloid disease should be avoided until more is known of their relation to this condition.

Intramuscular cortisone acetate 50 mg. daily does not prevent the healing of a bleeding duodenal ulcer (two cases only).

An average dose of 50 mg. a day of cortisone acetate continued for a year did not lead to any demonstrable abnormality in the adrenal cortex of a man aged 48.

Part of the cortisone used in this study was provided from a gift made jointly to the Medical Research Council and the Nuffield Trust by Messrs. Merck.

REFERENCES

Dobriner, K. (1952) Ciba Foundation Colloquia on Endocrinology. London; vol. I, p. 223.
Gallagher, T. F., Fukushima, D. K., Barry, M. C., Dobriner, K. (1951) *Recent Progr. Hormone Res.* 6, 142.
Hass, G. M., Huntington, R., Krumdieck, N. (1943) *Arch. Path.* 35, 226.
Lancet (1951) ii, 166.
Smetana, H. (1925) *Bull. Johns Hopk. Hosp.* 37, 383.

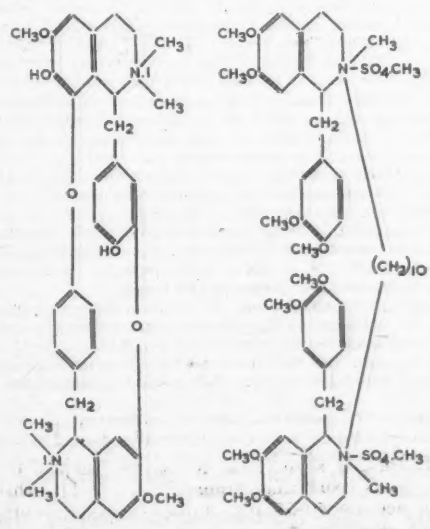
A NEW SYNTHETIC CURARISING AGENT

CLINICAL TRIAL OF COMPOUND 20 (LAUDOLISSIN)

R. I. BODMAN, M.B. Brist., D.A.
H. J. V. MORTON, M.D. Camb., D.A.
ANÆSTHETISTS, HILLINGDON HOSPITAL, UXBRIDGE, MIDDLESEX

W. D. WYLIE, M.B. Camb., M.R.C.P., D.A.
ANÆSTHETIST, ST. THOMAS'S HOSPITAL, LONDON

Taylor and Collier (1951), synthesising and investigating the muscle-relaxing properties of heterocyclic decamethylene *bis* quaternary ammonium compounds, produced one (Compound 20) which showed promise of being an effective substitute for *d*-tubocurarine in anæsthesia. This substance has been named 'Laudolissin.' Taylor (1952) described its chemistry, Collier and Macauley (1952) its pharmacology, and Bodman (1952) experiments with it in conscious volunteers. The structures of Compound 20 and *d*-tubocurarine are as follows:



Briefly, the workers cited above have established that Compound 20 is a true curarising agent, with a potency in man just half that of *d*-tubocurarine but with a duration of action slightly longer, and that it is antagonised by neostigmine.

Since no undesirable side-effects were detected during the work on volunteers, we decided to proceed with a trial in anæsthetised patients, and we record here our impressions of the clinical properties of Compound 20.

Compound 20 was substituted for the established relaxants in 186 procedures, as follows:

Operations	*No. of cases*
Partial gastrectomy	75
Cholecystectomy	14
Abdomino-perineal resection	6
Other major abdominal	47
Pneumonectomy	5
Valvulotomy	5
Other thoracotomies	9
Operations on the head and neck	10
Other major surgery	15
Total	186

Ninety-one patients were anæsthetised with nitrous oxide, with or without pethidine, and the remainder with cyclopropane. Induction was by thiopentone in all the cases.

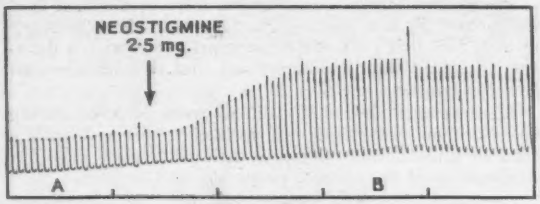
RESULTS

Muscle-relaxing Properties

In general the clinical impression gained has corroborated the experimental findings. A dose of 30 mg. of Compound 20 provided the same relaxation as 15 mg. of *d*-tubocurarine. But where the latter would have been expected to give adequate abdominal relaxation for thirty minutes, the relaxation with Compound 20 lasted forty minutes or more. Maximal abdominal relaxation was not evident until at least five minutes after the injection. The relative action on the abdominal muscles and the diaphragm seemed no different from that of *d*-tubocurarine. "Rectangular respiration" (Morton 1950) was often seen, and carried the same significance as when occurring with the established relaxant drugs.

Another aspect of a relaxant is its ability to paralyse the vocal cords. In a number of cases Compound 20 was given immediately after an initial dose of thiopentone, and intubation was attempted. In some cases relaxation of the cords was not obtained, even after several minutes and with doses which relaxed the abdominal muscles adequately. Conditions for intubating were certainly far less satisfactory than those obtainable with gallamine triethiodide. Consequently one inclined to the use of some other drug or technique for intubating, and reserved Compound 20 for maintaining surgical relaxation. A very satisfactory method was to use succinylcholine (with or without pethidine). Succinylcholine has a very short action, and does not seem to influence the effect of Compound 20 given after it; it has the additional advantage that the patient can breathe spontaneously while the preliminaries are being completed, before the surgeon actually starts the operation.

In experiments on animals Collier and Macauley (1952) demonstrated an antagonism between Compound 20 and succinylcholine, if given in that order: an appropriate dose of succinylcholine rapidly reversed the paralysis caused by Compound 20. With a larger dose a brief paralysis referable to the succinylcholine was followed by a rapid recovery from both drugs. We thus had reason to think that succinylcholine would be an ideal drug for producing additional relaxation for closure of the peritoneum. We have in fact used it with great success, in doses of 20–30 mg., on forty occasions after Compound 20, but as yet have been unable to obtain in anæsthetised patients a convincing demonstration of the antagonism seen in animals. On the other hand, we have seen no evidence of synergy between these two drugs, such as prolonged respiratory paralysis.



Effect of neostigmine on respiration of patient partially paralysed with Compound 20. Spirometer tracing, inspiration upwards. Tidal volume 300 ml. at A, 890 ml. at B.

In 13 cases we used ether for closure of the peritoneum, and it appeared to potentiate Compound 20.

There is no doubt about the antagonism in man between Compound 20 and neostigmine. The latter has been used on 35 occasions with satisfactory results. The accompanying figure illustrates such a case. But our present experience is insufficient for us to say whether this antagonism is greater or less than that between *d*-tubocurarine and neostigmine.

Side-effects and Incidental Properties

In 92 cases the pulse-rate and blood-pressure were recorded at five-minute intervals throughout the operation. In no case was there any change in either which could be attributed to Compound 20. In 3 cases electrocardiograms were made before, during, and after injection; they showed no change.

Of the signs which might be attributable to the release of histamine, bronchoconstriction was never evident, and no sudden or transient falls of blood-pressure were detected in association with the injection.

Experience with other relaxants led us to search for certain undesirable side-effects. Evidence of hæmolysis, such as hæmaturia and hæmoglobinuria, was not seen. The solution did not appear to irritate the vein, and there was no thrombosis or phlebitis. There was no action on the gut that could be seen by direct observation, and there was no ileus.

Compound 20 was not miscible with thiopentone, pethidine, or succinylcholine.

DISCUSSION

The properties of Compound 20 seem to be very similar to those of *d*-tubocurarine. So long as further trials with this drug confirm our findings, we think that Compound 20, of all the relaxants we have had occasion to use since their introduction into anæsthesia, could best take the place of *d*-tubocurarine for surgical relaxation.

The chief advantage of Compound 20 has not concerned us in this trial—it can be synthesised from materials readily available in this country.

SUMMARY

A clinical trial of a new muscle-relaxant has been described—Taylor and Collier's Compound 20, called laudolissin.

It has been used during general anæsthesia in 186 cases.

Its curarising properties are very similar to those of *d*-tubocurarine, except that its action lasts longer.

No important undesirable side-effects were detected.

Messrs. Allen Hanburys supplied the laudolissin used in this trial.

ADDENDUM

Since this paper was written Compound 20 has been used in a further 50 major procedures without incident.

REFERENCES

Bodman, R. I. (1952) *Brit. J. Pharmacol.* 7, 409.
Collier, H. O. J., Macauley, B. (1952) *Ibid*, p. 398.
Morton, H. J. V. (1950) *Anæsthesia*, 5, 112.
Taylor, E. P. (1952) *J. chem. Soc.* p. 142.
— Collier, H. O. J. (1951) *Nature, Lond.* 167, 692.

SPONTANEOUS SEPARATION OF AN INTUSSUSCEPTION

FAUSET WELSH
M.B. Birm., F.R.C.S.
SURGEON, BIRMINGHAM UNITED HOSPITALS

SPONTANEOUS separation of an intussusception is described in the textbooks as a possibility, but it is rare. The case described here ran a subacute course after the onset, and the pathological processes were verified by recovery of the separated bowel and by laparotomy after the separation. The case was demonstrated at a meeting of the Midland Medical Society on Jan. 31, 1951, and three members at the meeting described other cases of spontaneous separation of an intussusception.

CASE-RECORD

An engineer, aged 74, of sturdy physique and vigorous habit, was taken ill on Sept. 4, 1948. He complained of upper abdominal pain while having his tea. Within a few minutes it became very severe, and he collapsed. He was found by Dr. C. Ramsdale shortly afterwards to be collapsed, grey, cold, with a clammy skin, almost pulseless, and with cyanosis of the lips, nose, ears, and fingers. His abdomen was soft and not tender, and no abnormality could be felt. Coronary thrombosis was provisionally diagnosed, and he was thought to be dying. Nikethamide and morphine were injected, and amyl-nitrite inhalations were given. After an hour he recovered sufficiently for Dr. Ramsdale to leave him.

On examination on Sept. 5 his circulation had fully recovered, but he was vomiting bile-stained fluid, and his abdomen was tense and distended, though not tender. He complained of vague pain in the lower abdomen. The diagnosis was altered to mesenteric thrombosis. I saw him that evening and agreed with this. The patient refused operation, and it was not strongly advised.

Progress.—During the next three days he remained distended, constipated, and vomiting. On one occasion the vomit had a fæcal smell. His temperature rose to 100°F on Sept. 9. On Sept. 10 he was transferred to hospital, and a good result was obtained from an enema. He continued to vomit bile-stained fluid. Dehydration was corrected with saline solution per rectum. I saw him again on Sept. 12 and found him very distended, and considered the possibility of a volvulus. A flatus tube was passed with a good result. His distension decreased, and vomiting became much less. He was walking about the ward after Sept. 24. Up to Oct. 2 he remained in hospital, and a gradual improvement took place, punctuated by occasional attacks of vomiting. Bowel action became regular, and he had a moderate appetite. Pain disappeared, and his abdomen remained slightly distended, but soft and not tender. The day after he went home he had a little diarrhœa, which continued with occasional vomiting. By Oct. 10 he had much improved, and did not vomit. On this day he had an excellent bowel action in the morning, and passed 2 ft. of macerated small intestine. Pathological examination of the gangrenous bowel which was passed showed a simple polypus. Next day vomiting of dark-stained fluid began again, and on Oct. 12 and 13 was profuse. He was now getting intestinal colic, and his abdomen was distended. On admission to hospital on Oct. 14 he was in fair condition, though rather sallow and dehydrated. His blood-pressure was 180/80 mm. Hg, temperature 98°F, and pulse-rate, 80. A plain radiograph of the abdomen showed dilated coils of jejunum and ileum.

Operation.—At laparotomy on Oct. 15, distended gut was found. A volvulus of the jejunum was corrected, and the site of an obstruction was discovered 3 or 4 ft. proximal to the ileocæcal valve. At this point a stricture with surrounding adhesions was discovered. Side-to-side anastomosis was done.

Progress.—The patient made an uninterrupted recovery. He drove his own car to the meeting in January, 1951, where his case was demonstrated.

COMMENTS

In the ensuing discussion at the Midland Medical Society, Dr. H. W. Hickman reported that he had seen

a young Indian vagrant who was operated on for ileo-cæcal intussusception which recurred after twenty-four hours. Conservative measures were adopted, and the patient passed the intussusception. A subsequent barium enema showed the appearances of an ileo-transverse anastomosis.

Mr. K. O. Parsons reported a case of intussusception of the pelvic colon in a patient who presented with gangrenous bowel protruding from the anus. He had been previously diagnosed elsewhere as a case of prolapse. The patient passed the intussusception five weeks later. A barium enema showed no signs of the anastomotic level.

Mr. Wilfred Mills reported that he had been called to a patient in a mental hospital who was said to be "passing his uterus through his rectum." There was some reason for this description because the prolapsed bowel closely resembled a patulous cervix. Again this intussusception sloughed away, leaving a normally functioning bowel.

In children with intussusception, initial shock is well known, and recognised by quietness and pallor. In the present case in an adult, shock was disproportionate to the pathological condition present. An extreme degree of shock is not commonly seen in acute intestinal obstruction caused by strangulated hernia, or even by impaction of large gall-stones. Acute intestinal obstruction appears in this case not to have been complete until after the separation of the intussusception, when one would have expected recovery. It is possible that complete obstruction was caused by rapid cicatrisation at the site of separation, and was delayed by the presence of the bulky gangrenous mass.

One wonders if diagnosis could have been made in the early stages by barium contrast filling and X rays, but it is doubtful if operation would have been strongly urged even in the presence of an accurate diagnosis, because of the absence of complete obstruction. The total absence of blood from the stools at all times is noteworthy.

Reviews of Books

Eugenics: Galton and After

C. P. BLACKER, M.C., G.M., M.A., M.D., F.R.C.P., general secretary, Eugenics Society. London: Duckworth. 1952. Pp. 349. 25*s*.

Dr. Blacker has combined a biography of Sir Francis Galton with a review of the development, after Galton's death in 1911, of the "science, practice and religion" of eugenics. In his description of the person and work of this remarkable cousin of Darwin, Dr. Blacker follows closely Karl Pearson's biography, and the first third of the book is a reliable account of the many interests of a highly gifted and well-connected Victorian gentleman. His account of developments since 1911 gives a better view of what Galton accomplished than can be found anywhere else, and sets it in a framework of modern views about genetics and eugenics. It would be a mistake, however, to regard the book as a detached and academic survey. It is written from a personal standpoint which many do not share. Since eugenics (and even genetics) offer such controversial themes this was inevitable, and the reader must allow for it. In addition, a fair amount of the controversy in this country on national intelligence and kindred issues is reported, and there are informative accounts of the demography of the peoples of the earth, of some recent general developments in genetics (but not in human genetics), and of methods of ascertainment.

The Scientific Paper

2nd ed. SAM F. TRELEASE, Columbia University. London: Baillière, Tindall, & Cox. 1951. Pp. 163. 20*s*.

AUTHORS who worry about their manuscripts, and would gladly make them less of a burden to editors and more of a joy to readers, will be much helped by this little book. It deals with every aspect of collecting and presenting the results of scientific work: the use of the library, treatment of data, reliability and significance of measurements, the actual writing and the choice of headings, logical presentation, how to maintain interest, revision, typescript, correction, the estimation of length, good usages, tables, illustrations, the ways of editors, and proof-reading. Experienced writers will not find anything unfamiliar, but few books cover the problem so completely as this one. The introduction, Mr. Trelease says, should state the problem, describe its condition at the beginning of the study, tell the reasons for investigating it, and give the purpose, scope, and general method of the investigation. He also thinks it should state clearly and definitely the most significant result of the investigation; for this not only enables the reader to distinguish essential from non-essential evidence, but makes the writer face squarely at the outset what it is that he really wants to say—whether, indeed, he has anything to say. Like other advisers on scientific writing, he emphasises the need for numerous revisions. It is true that a revised manuscript is likely to be better than one which is "dashed off" and dispatched without revision, but there is a limit to the number of useful revisions: some much-revised papers show that their writers have grown sick of the sight of them and are no longer interested in correcting their faults. Before he begins to write, an author should plan his paper so that it conforms to the layout of the journal of his choice. He should then write with a two-inch margin and three spaces between the lines. He can do a great deal of correction on such a script without rendering it illegible to an intelligent typist. Two candid friends of good critical ability, knowledge of the subject, and experience of publishing papers should independently edit and freely comment on copies of the draft; and the author should weigh their observations, think his own second thoughts, and transfer the result to his correction copy. This should be retyped and sent to the editor. If writers would observe these sensible rules it is probable that the editorial staff of scientific journals would live much longer and look much younger than is usual for persons of this kind.

Atlas of Tumor Pathology

Fascicle 9. RUPERT A. WILLIS, M.D., F.R.C.P., professor of pathology, University of Leeds. Pp. 58. 50 cents. Fascicle 16. PHILIP M. LE COMPTE, M.D., pathologist, Faulkner Hospital, Boston, Mass. Pp. 40. 45 cents. Fascicle 18. HANS G. SCHLUMBERGER, M.D., professor of pathology, Ohio State University. Pp. 88. 75 cents. Fascicle 29. HOWARD T. KARSNER, M.D., medical research adviser, Bureau of Medicine and Surgery, United States Navy. Pp. 60. $1.00. Fascicle 34. FRED W. STEWART, M.D. Pp. 114. $1.10. Washington: Armed Forces Institute of Pathology. 1950 and 1951.

THESE helpful monographs are published at a reasonable price by the Armed Forces Institute of Pathology, under the auspices of the National Research Council, and are sponsored by various bodies, including the American Cancer Society and the National Cancer Institute of the United States Public Health Service. They form part of an atlas of tumour pathology, and the illustrations are very good though the subject matter is brief. They contain a surprising amount of information nevertheless, and contrive to survey prognosis and treatment into the bargain.

The fascicle by Prof. R. A. Willis is on teratomas, which he defines as neoplasms composed of multiple tissues foreign to the part in which they arise. He believes that they may represent areas of tissue which, during early embryonic development, escaped from the action of the primary organiser, and adduces evidence against the popular view that they are embryomas or distorted fœtuses, derived either from included twins of the bearers or from parthogenetic proliferation of the host's own germ cells.

Dr. Philip M. Le Compte writes on tumours of the carotid body and related structures. Since most carotid-body tumours are both clinically and histologically benign, he

favours a diagnostic biopsy only. The surgeon who decides to operate should realise that "he has one chance in three of killing his patient and if the patient survives, about eight chances in ten of leaving him with some kind of temporary or permanent neurological disturbance." For tumours of the glomus jugulare, Le Compte recommends radical tympano-mastoidectomy when the diagnosis is established. He also gives brief accounts of tumours of the aortic bodies, and tumours arising in the ganglion nodosum of the vagus, and believes that there are probably two unverified instances of neoplasms arising in the paraganglion ciliare. Tumours of the chemoreceptor system are in general radio-resistant.

In his account of tumours of the mediastinum, Dr. Hans G. Schlumberger does not include an account of tumours of the thymus, œsophagus, heart, or pericardium; but he discusses the histogenesis of the many others met with in this situation, including those arising from misplaced organs. Every mediastinal tumour not known to be metastatic, he says, should be submitted to biopsy before it is irradiated; for this not only establishes the diagnosis but makes it possible to avoid those post-irradiational tissue changes which often increase the difficulty of surgical removal.

Dr. Howard T. Karsner, writing on tumours of the adrenal, includes an account of the tumour-like myelolipoma. He holds that a diagnosis of phæochromocytoma is not valid without a positive chromaffin reaction, because polygonal cells may be numerous in cortical adenoma while cells which resemble those of the cortex occur in phæochromocytoma.

The excellent section on tumours of the breast is written by Dr. Fred W. Stewart. Primary mammary cancer can occur, he says, in any postpubertal breast: in fact, with increasing experience a pathologist may employ the term "pre-cancerous" less and less. The youngest patient he had seen was twenty; the oldest were identical female twins over ninety years of age. Gross anatomy and the extent of disease, he holds, far outweigh in importance microscopical classification, although confirmation of the two may yield significant information. With involvement of the basal axillary group of nodes only, Dr. Stewart has found a 65% survival-rate at 5 years. If the midgroup are involved the survival-rate falls to 45%, while if the apical axillary nodes are affected the survival-rate is only 28%. The so-called medullary type of carcinoma with a lymphoid stroma has a better survival-rate than the average scirrhous cancer: in 5 years only 11·5% had died of their disease in the former group, as against 56% in the latter group.

Management of the Newborn

ARTHUR HAWLEY PARMELEE, M.D., professor of pediatrics, University of Southern California. Chicago: Yearbook Publishers. 1952. Pp. 358. $7.

THIS excellent book on the newborn infant will be a welcome addition to the shelves of pædiatricians and obstetricians. Professor Parmelee has had intensive experience of the newborn for many years, and his approach is physiological and clinical. He is a keen and accurate observer, and he has produced a "story of the newborn" which is a pleasure to read. Fully half of the book deals with the normal infant, and the remainder is a comprehensive account of abnormalities and diseases of the newborn. The 83 illustrations are good, but such a valuable book is worthy of many more. It is a pity that American books are now so expensive in this country, but no-one who has regular care of the newborn can afford to be without this one.

Connective Tissues

Transactions of the Second Conference, May 24 and 25, 1951. Editor: CHARLES RAGAN. New York: Josiah Macy, Jr., Foundation. 1952. Pp. 190. $3.50.

THE second Josiah Macy conference on connective tissues has produced a volume even more interesting than the first; but when experts confer, new words and unfamiliar concepts, likely to be above the heads of some of us, are often taken for granted. Some small editorial explanatory notes in the present volume are therefore helpful, and more of them would be welcome in later books of the series.

Of the five main topics pain mechanisms in connective tissues, discussed by Travell, is the only one which represents the clinical approach. The other four are of more fundamental nature. Porter's valuable contribution on repair processes in connective tissue is illustrated by a series of beautiful electron micrographs showing the stages of collagen-fibre formation in relation to the cell-surfaces of chick embryo fibroblasts in tissue culture. Morrione deals with the regression of scar-tissue as seen in recovery from experimental cirrhosis of the liver, and advances several ideas which may bear on restoration of the normal state after fibrous-tissue healing in various other maladies, such as rheumatic heart-disease and nephrosclerosis. In discussing the chemical morphology of elastic fibres, Lansing is concerned with the chemistry of the individual fibres and the reasons for their spiral structure, which can be seen under both the light and electron microscopes. Gersh treats mainly of alterations in the appearance and staining reactions of ground substance in relation to the action of hormones or the mechanism of allergy, and also discusses its origin and fate.

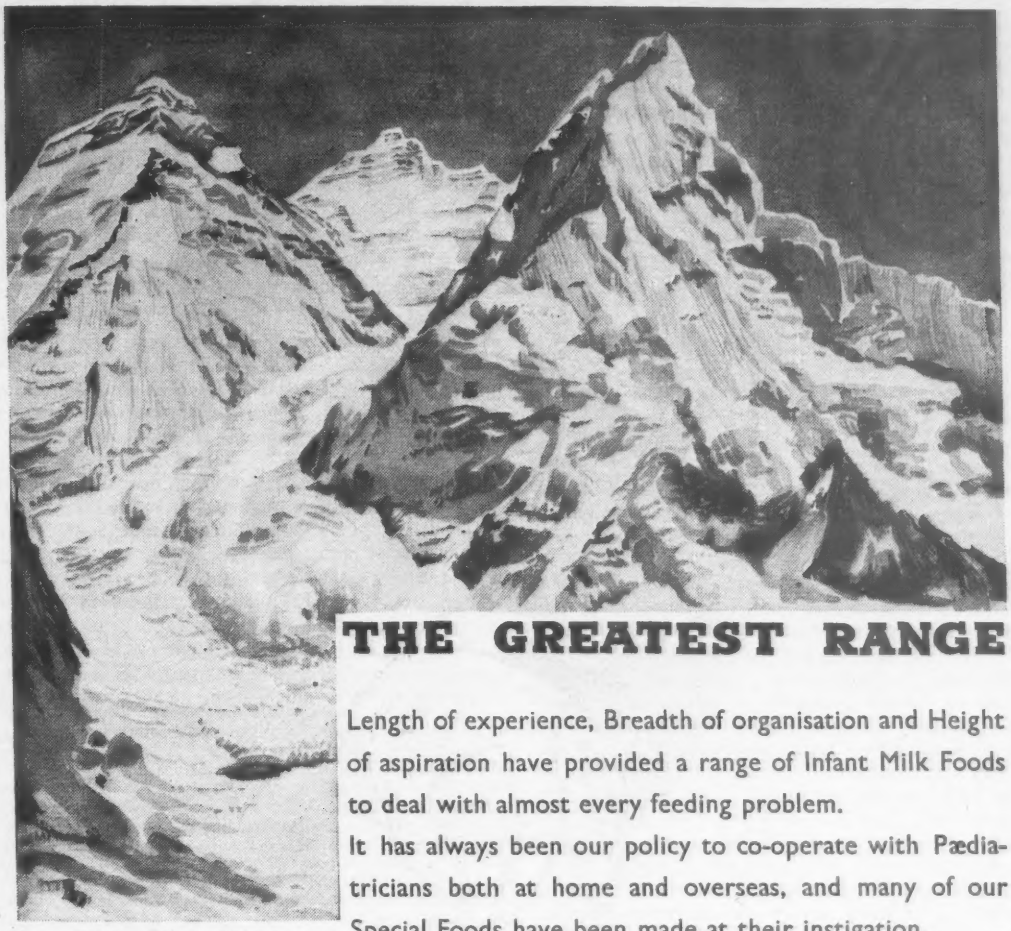
Disease in Old Age

ROBERT T. MONROE, M.D. From the Medical Clinic of the Peter Brent Brigham Hospital and department of medicine, Harvard Medical School, Boston, Massachusetts. Boston: Harvard University Press. London: Oxford University Press. 1951. Pp. 407. 32*s.* 6*d.*

Dr. Monroe has made an elaborate analysis of the medical records of 7941 patients over the age of 61 who were admitted to hospital during the years 1913–43. The wealth of the clinical material he describes is impressive; though it would have been more useful if he had compared the incidence of disease in his patients and in those of lower age-groups. He points out that hospital management and practice must nowadays be adjusted to patients in the higher age-groups; for whereas, in 1913, 1 in every 16 patients admitted to hospital was over the age of 61, in 1943, 1 in every 5 patients admitted was of this age—an increase of 200% in 30 years. To those who hold that continued useful employment assists in the maintenance of physical and mental health, Dr. Monroe's figures are depressing, for 92% of men between the ages of 61 and 65 were in employment during the first decade under review, compared with 66% during the last. These figures help to confirm the trend which has been observed in surveys carried out both in this country and in the U.S.A. Dr. Monroe's views on the management of elderly patients are refreshingly humane, and he puts forward a sensible scheme for a comprehensive service for elderly persons, organised by the community, which would ensure an adequate supply of beds of various categories, linked with a central hospital. He emphasises the value of the geriatric clinic, and ends with a plea for an "age centre." This would include a supply of one- and two-roomed flats for about 400 people, where adequate medical and social services would be available.

Hospital Organisation and Management (4th ed. London: Faber & Faber. 1952. Pp. 1782. £8 8*s.*).—This standard work, first published in 1927, is now very portly. Captain J. E. Stone has amplified the facts and data gathered during many years of active work in the hospital field with numerous references to American experience, and to the changes brought about by the National Health Service Act. This has not been offset by sufficient compression and pruning. The appendices, too, which take up as much as 300 pages, could be shortened. Nevertheless this is a very good account of the development of the British hospital system, and of methods of hospital management. All departments of hospital organisation are covered, and the chapters on the law relating to hospitals could not be improved.

Applied Physiology (9th ed. London: Oxford University Press. 1952. Pp. 1190. 50*s.*).—The appearance of the new edition is as startling as that of an old friend who returns from a holiday with an unexpected moustache; but there can be no misgivings about Prof. Samson Wright's book. With the aid of Prof. Montague Maizels and Mr. J. B. Jepson, D.PHIL, he has rewritten more than half the text, and rearranged the presentation in drastic fashion. Though past readers may take time to find their way about again, they will readily agree that the new sequence of subjects is an improvement, starting as it does from "the outstanding generalization of physiology"—the constancy of the internal environment. Some 200 new illustrations have been added. What is virtually a new book will enjoy an even greater popularity.



THE HIMALAYAS

THE GREATEST RANGE

Length of experience, Breadth of organisation and Height of aspiration have provided a range of Infant Milk Foods to deal with almost every feeding problem.

It has always been our policy to co-operate with Pædiatricians both at home and overseas, and many of our Special Foods have been made at their instigation.

If you have any feeding problems, we shall be only too happy to give you any possible help, by discussing production of additional special foods.

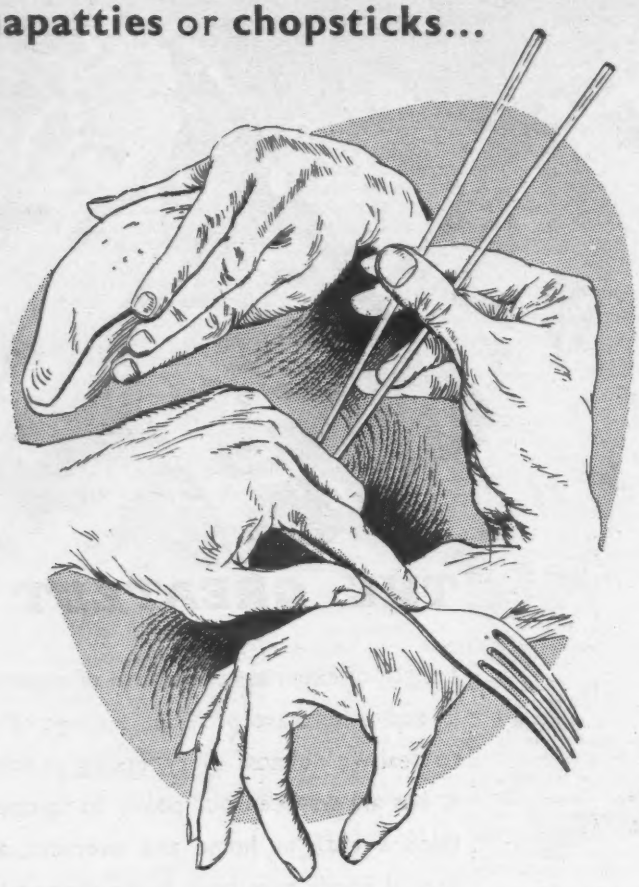
Full details of all our products, with analyses and indications, are given in our Medical Handbook, obtainable on request from the Medical & Research Department, Cow & Gate House, Guildford. CLINICAL SAMPLES will also be sent.

COW & GATE MILK FOODS

GUILDFORD SURREY

4912

chapatties or chopsticks...



forks or fingers...

Though methods and menus vary, *nutritional* needs are much the same the world over. And the body's need of protein is just as imperative in Pakistan as it is in Peckham! Wherever you are, there is a sure and simple way of giving your patients the extra protein they need —by prescribing CASILAN. 90 per cent protein, flavourless, and economical in use, CASILAN is as easily prepared in the home as in the hospital kitchen. It blends perfectly into almost any dish your patient fancies or you permit... is a 'good mixer' in every sense.

WHOLE PROTEIN **Casilan** Trade mark *8-oz. containers*

Research Laboratories: Manufacturers of medical products and foods. Agents or associate companies in almost every country in the world.

GLAXO LABORATORIES LIMITED, GREENFORD, MIDDLESEX, ENGLAND

THE LANCET

LONDON: SATURDAY, SEPT. 13, 1952

Family Size and Natural Selection

FROM time to time we should turn our attention from the triumphs of sanitary and medical science to consider the ultimate effects of these successes on the evolution of the human species. Bacteriologists and virologists are used to thinking of genetic constitution in terms of variation in the host's resistance and the parasite's virulence; and Sir MACFARLANE BURNET, F.R.S.,[1] has sounded a salutary warning to those who think of human health purely in terms of environment. Applied microbiology, he notes, has overcome the high death-rate from infectious disease which has hitherto been a feature of urban civilisation; while the food-shortage that would otherwise have ensued has been largely prevented by deliberate restriction of the number of children.

"Unfortunately this is not a satisfactory long-term solution of the problem that we have created by abolishing infective disease. If we ensure in general terms that each pair produces two children both of whom reach reproductive age and that the process continues indefinitely, we must inevitably come up against the problem of genetic deterioration. . . . The whole structure of the evolutionary process depends on the fact that mutation is constantly occurring and that only by a highly selective winnowing of the various gene-combinations that arise can evolutionary progress or even maintenance of quality occur. The vast majority of gene changes must of necessity be disadvantageous to the carrier. To maintain the normal character of the species every appearance of a deleterious mutation must be balanced by a 'genetic death.'"

The geneticist expects a constant tendency for the frequency and severity of a disease to return to a level at which the disadvantageous genes predisposing to the disease that are lost in each generation, from the relative infertility of those affected, will balance the new genes of this type appearing in each generation by mutation. Deterioration in environmental conditions will temporarily increase the mortality from the disease, but this fiercer selection will in time decrease the number of genes in the population predisposing to the disease until, without further change in the environment, mortality is brought back to the level which balances the constantly recurring new mutations. In the same way environmental improvement, such as a better method of treatment, will be followed by decreased mortality and accumulation of genes predisposing to the disease until once again the death-rate reaches the equilibrium level. Just how many deaths from diphtheria, for example, represent the equilibrium point it is impossible to say; this point will depend on the number of genes concerned, their mutation-rates, and the specificity of resistance to diphtheria. But, as with several other infectious diseases, deaths from diphtheria in this country are below equilibrium level after a century of adjustment of an originally rural population to city life during which mortality was much above this level. Immunisation against diphtheria is at present effective, but the capacity to respond to the toxin may well depend on past racial selection for resistance to the organism, and may be progressively lost after some generations in which there are no deaths from the disease. Where living organisms are used for immunisation, as in vaccination, the relative safety of the procedure probably depends on generations of selection for resistance; as the effects of this selection are lost, universal vaccination may come to cause as many deaths as did smallpox in a community long and freely exposed to infection by this virus. Few diseases will ever be exactly at the equilibrium point; and changes in bacterial and viral virulence will also for the time being upset the equilibrium. But in the long run environmental improvements, with one exception, are not by themselves likely to alter the mortality from any particular disease; they will merely lead to an increased morbidity-rate balancing a reduced case-mortality. The single exception is the elimination of the agent causing the disease. This is possible with some infectious diseases, and when it has been achieved genetic deterioration for resistance to the disease becomes irrelevant. But the number of diseases which can be controlled in this way seems limited—and this is true even of infectious diseases.

Human genetics is a new science, and little is known about the amount of selection needed to maintain equilibrium against the sum of disadvantageous mutations. One expert guess, by Professor MULLER,[2] is that one gamete in five contains a new disadvantageous mutation. Whatever the selection needed, the human species has in the past more than held its own; and so selection must have been adequate. Until recently, however, there has been plenty of material on which selection could operate. At all periods except those of the most rapid population growth, less than half of natural families averaging six or seven children survived to have children in their turn. While some of these deaths may have been purely accidental, most were probably related in some way to the genetic constitution of the child or his parents. It is unthinkable that there should be a voluntary return to natural selection of this intensity. Fortunately, as GALTON noted more than fifty years ago, as knowledge of human genetics grows, artificial selection is likely to prove both more humane and more efficient than natural selection; and GALTON coined the term "eugenics" for artificial selection of this kind. If genetically ill-endowed individuals, kept alive by medical science or public hygiene, plan a family size 50% below replacement-rate, this gives as much gene-elimination as does the premature death of half of them. Further, artificial selection will be able to take account of the possession of genes in the heterozygous state, which when recessive are not subject to natural selection. In our kind of democracy eugenics must depend on self-selection by responsible parents, influenced in their choice of family size by genetic considerations. The present practice of planning families of only 2–4 children, with large families coming from the diminishing proportion of the population incapable of planning, probably

1. *Med. J. Aust.* 1952, 1, 801.

2. Muller, H. J. *Amer. J. hum. Genet.* 1950, 2, 111.

provides insufficient scope for the maintenance of genetic standards, even with the best selection of those who aim at 4 and those who aim at 2 children. Probably even the family-size distribution suggested by the Swedish Commission on Population, with 33% of 3-child families, 27% of 4-child families, and 5% of 5-child families, though it would keep up the size of the population, would not provide adequate differentials to maintain genetic quality. General OSBORN [3] has suggested that, for this, family size should be distributed as follows: 19% 0 children, 15% 1 child, 16% 2 children, 18% 3 children, 18% 4 children, and 14% 5½ children.

Parents cannot be coerced into having children, and at first sight such a high proportion of large families might seem unattainable, since to achieve 14% large families a much higher percentage must aim at a large family. But in the next few generations in countries with planned families there will be intense selection for genes favouring genophilia—the desire for, and delight in, children. With few children conceived as the accidental by-product of sexual activity, it will mostly be genophilic impulses that decide family size. Those well-endowed in this respect will contribute an increasing proportion of coming generations; and those who aim at only 2 children for eugenic or other reasons will mostly be doing so unwillingly, with a sense of responsibility, and will need to find other ways to express their genophilic impulses. As some of the environmental causes of diseases are entirely eliminated, and it becomes no longer necessary to maintain selection for freedom from, or resistance, to these diseases, it will be possible to use selection with the much more attractive aim of improving human genetic standards for qualities which are desirable but not directly related to mere survival—for example, general and special types of intelligence, artistic gifts, and, more important still, worth-while qualities of character. To quote BURNET once more: "Whatever we feel about the present social and political impossibility of any programme of practical eugenics, we can be quite certain that decade by decade the importance of action will be progressively more widely realised. Sooner or later action will have to be taken and it is our responsibility to initiate the process of accumulating valid knowledge on which eventual action can be soundly based. I repeat that this is the most important task of medical research today."

Prognosis in Asthma

THE prognosis of asthma, like that of many other recurrent conditions, is still largely a mystery. Long-term follow-up studies are rarely completed, since the disorder waxes and wanes over the years, the patient tries one doctor or hospital after another, and, perhaps from delicacy, he may not answer the follow-up letter.

WILLIAMS [4] observes that in the twenty years between 1930 and 1949 the death-rate from asthma in England and Wales was 7·07 per 100,000 of the population, compared with 1·65 in the United States. In England and Wales during the years 1938–49 deaths from asthma amounted to 0·6% of all deaths, accounting for roughly 3000 deaths per annum; approximately 96% of those dying from this cause were over 30 years of age. WILLIAMS cites 110 reported cases of death from asthma in patients over 30 years of age. Of these patients 51 (46%) had had asthma for less than 5 years, and in this latter group 44 (87%) died within 2 years of the onset. The remaining 59 (53%) had had asthma for more than 5 years—including 36 (33%) for more than 10 years, and 16 (18%) for more than 20 years. WILLIAMS also shows that deaths from asthma have a seasonal distribution corresponding closely with the incidence of respiratory infections and bronchitis. BULLEN [5] studied a group of 176 asthmatics who died in hospital in a town in the United States. Of these patients 94 died during attacks of asthma. Of the total of 176 more than half died within 10 years of the onset, and one-fifth within 5 years. Of 13 patients in whom asthma started before the age of 5 years, 6 died within 1 year and 4 within 7–11 years. Nearly half the patients survived beyond the age of 60, but those whose asthma began when they were over 40 years of age had a much worse prognosis than those who first had symptoms before the age of 25. In a series of 500 asthmatics seen in private practice only 9% first had symptoms after 40 years, compared with 22% of the 176 patients who died in hospital. Thus hospital statistics, as might be expected, probably give an unduly grave impression of the proportion of all asthmatics who die of the disease.

RACKEMANN and EDWARDS [6] give some basic facts on prognosis in a twenty-year follow-up of 688 asthmatic children, most of whom were seen in private practice. All but 29 were traced by letter or interview, so that over 95% are included. 449 were first seen before the age of 13, while the remaining 239, though they became asthmatic before that age, were first seen later. Of the 449 children 4 (less than 1%) had died of asthma by the late 20s, whereas of the 239 older patients 6 (about 2·5%) had died after 20 years—1 at the age of 28, and the other 5 at ages between 40 and 50. Among the 449 children seen before the age of 13, boys outnumbered girls by about 2 to 1. In treatment the most important factor seemed to be withdrawal of feathers, animal dander, "inhalants," and certain foods, rather than specific desensitisation. Some 31% lost their asthma entirely during their 'teens, though not necessarily at puberty. Another 19% remained free of symptoms so long as they avoided the specific allergen to which they were still sensitive; and 21% were free of asthma but had developed another allergic condition, hay-fever being by far the most common. Thus about 70% of the children more or less lost their asthma during their 'teens. About 26% of the patients still had asthma, but only 10% had severe symptoms. One-fifth of the children had negative skin tests, and their attacks were associated with respiratory infections; whereas in the remaining four-fifths the disorder was ascribed to allergy. In the group of 239 patients who were first seen after the age of 13, the results were not so good. After 20 years about 22% were symptom-free, 26% were still sensitive but

3. Osborn, F. Preface to Eugenics. New York, 1940; p. 248, table 51.
4. Williams, D. A. Proceedings of the first International Congress of Allergy. 1952.
5. Bullen, S. S. *J. Allergy*, 1952, **23**, 193.
6. Rackemann, F. M., Edwards, M. C. *New Engl. J. Med.* 1952, **246**, 815, 858.

remained well when avoiding allergens, and 8% were free of asthma but had developed other allergies; about 10% were left with mild, and 25% with severe, asthma. Of 12 patients in whom polypoid sinusitis developed, 4 had died of asthma; so gross nasal disease is a bad prognostic sign.

The 688 cases are placed in five ætiological groups, depending on the clinical features and results of skin tests. Animal allergens account for 190 cases (roughly 29%), and foods for 48 cases (7%) mostly in young children with associated eczema. Pollen sensitivity was regarded as the important factor in 42 cases (5%), and mixed or unidentified allergens in 296 cases (42%). Skin tests were negative in 112 cases (16%), in most of which bacterial infection was thought to be the important cause. Of 86 children who had hay-fever, only 2 were free of symptoms by adult age. In 42 the hay-fever was mild; but in 28 (about a third) it was severe, and of these 13 developed pollen asthma and 7 asthma at any season. In 4 cases eczema recurred in adult life.

This important investigation shows that one child in four treated by a very experienced physician has continued to have asthma after 20 years of age, and about 2% actually died in asthmatic attacks. The proportion of failures is undoubtedly higher in children treated by palliative drugs alone. The prognosis is much graver in patients developing asthma when past 30 years of age; for then infection of the respiratory tract is common and may persist. This study should prompt us to discard the complacent belief that palliative treatment usually suffices. The asthmatic child or adult should be carefully investigated *at the onset* of symptoms and a rational régime instituted forthwith. This should include a serious effort to free the bedroom of dust and inhalant allergens, and to train the patient in remedial breathing exercises under the supervision of a physiotherapist.

Of Mice and Men

THE mills of virus research grind slowly, yet they grind exceeding small. Recent research on smallpox is a most instructive example of the tortuous, winding path that sometimes leads to practical progress. The story is a fascinating one, beginning with the discovery by HIRST [1] and MCLELLAND and HARE [2] that influenza virus agglutinates red cells from a number of animal species. It was soon found that vaccinia,[3] smallpox,[4] and other pox viruses also had this unusual property. The pox viruses have the distinctive property of agglutinating red cells from only 20–50% of fowls; and in 1946 BURNET and BOAKE [5] found that ectromelia virus also had this property and in other ways, too, resembled the pox viruses; and they proposed that ectromelia should be renamed mousepox virus. The next step can be readily pictured. Smallpox could not be studied easily in the laboratory, but mousepox might provide an excellent model of the behaviour of smallpox virus. FENNER was quick to seize the opportunity of learning about the epidemiology of mousepox, and the result was a series of painstaking and brilliant studies.[6] Before long practical applications [7 8] justified this roundabout road to progress.

When GLEDHILL and ANDREWES [9] described a virus which caused hepatitis in mice, it was at once apparent that this might be another instance of the way in which the study of a disease in mice may throw light on some of the difficult problems of epidemiology in man. Mouse hepatitis is an odd disease. The virus is apparently carried in the blood of one breed of mice (P.) which remain symptomless, but it can be transmitted to another breed (V.S.) which contract fatal hepatitis. The viruses of mouse hepatitis and of serum hepatitis in man have somewhat different properties, but superficially the analogy between the two diseases is striking. On an earlier page Dr. GLEDHILL, Dr. DICK, and Dr. ANDREWES describe further researches on mouse-hepatitis virus and reach the rather surprising conclusion that mouse hepatitis is caused by the combined action of two agents, which singly are non-pathogenic but cause fatal hepatitis when present together in the correct proportions. They were led to this conclusion by the results of experiments on the curative effect of terramycin on mouse hepatitis. From mice which had been inoculated with mouse-hepatitis virus and terramycin, a transmissible filterable agent was recovered which was non-pathogenic but immunised against mouse hepatitis; this agent was called S. (for stable). A second agent, called L. (for labile), was recovered by growing mouse-hepatitis virus at high dilution. L. and S. are both transmissible filterable agents which separately are non-pathogenic but together cause fatal hepatitis. We shall have to wait for further information on the lesions produced by these agents and any serological reactions that they evoke, and also for a final decision as to whether they are relations or just friends. Meanwhile the concept of viruses hunting in pairs should arouse great interest. There have been many well-substantiated reports of the simultaneous isolation of poliomyelitis and Coxsackie viruses from patients with poliomyelitis; and the interpretation by MELNICK et al.[10] that the Coxsackie virus may tip the balance towards paralysis accords with the known facts and with the findings in mouse hepatitis.

Experimental work with the viruses of hepatitis in man has also made big strides. Progress in this field still depends on that most unreliable laboratory animal, the human volunteer; and assessment of the results is always more difficult than with mice, which have learnt to say "yes" and "no" but not "maybe." Recently, however, DRAKE and his co-workers [11] have reported that a skin-testing antigen prepared from infective-hepatitis virus apparently protects people during an epidemic of infective hepatitis. In another paper these workers describe [12] results which lead them to believe that they have propagated the serum-hepatitis virus in eggs. Then again γ-globulin has been used successfully for protection against infective hepatitis. It seems, therefore, that the efforts of mice and men are not vain.

1. Hirst, G. K. *Science*, 1941, **94**, 22.
2. McLelland, L., Hare, R. *Canad. J. publ. Hlth*, 1941, **32**, 530.
3. Clark, E., Nagler, F. P. O. *Aust. J. exp. Biol. med. Sci.* 1943, **21**, 103.
4. North, E. A. *Ibid*, 1944, **22**, 105.
5. Burnet, F. M., Boake, W. C. *J. Immunol.* 1946, **53**, 1.
6. Fenner, F. *Lancet*, 1948, ii, 915.
7. Downie, A. W., McCarthy, K., Macdonald, A. *Ibid*, 1950, ii, 513.
8. MacCallum, F. O., McPherson, C. A., Johnstone, D. F. *Ibid*, p. 514.
9. Gledhill, A. W., Andrewes, C. H. *Brit. J. exp. Path.* 1951, **32**, 559.
10. Melnick, J. L., Kaplan, A. S., Zabin, E., Contreas, G., Larkum, N. W. *J. exp. Med.* 1951, **94**, 471.
11. Drake, M. E., Ward, C., Stokes, J. jun., Henle, W., Medairy, G. C., Mangold, F., Henle, G. *Ibid*, 1952, **95**, 231.
12. Henle, W., Drake, M. E., Henle, G., Stokes, J. jun. *Arch. ges. VirusForsch.* 1952, **4**, 612.

Annotations

TROPICAL FATIGUE

IN the past the danger of tropical diseases was sufficient reason for Europeans to be advised to avoid long periods in the tropics. The gradual conquest of these diseases has largely removed this danger, but there is still a widespread belief that life in the tropics can lead to physical deterioration. The term "tropical fatigue" has been introduced to describe a decline in efficiency attributable to environmental conditions. The nature of this failure has often been discussed, but there has been little systematic study. During the war, however, tropical fatigue assumed considerable importance, especially in the Pacific area, and an investigation was carried out in the Australian and New Zealand Armed Forces; Lee and Macpherson have given a detailed account of this work.[1 2] The first question that needed answering was: Does tropical fatigue exist? And the second: If it does, is it essentially physiological or psychological?

The investigations were carried out in the field in New Guinea and the adjacent islands. Some 1800 men, whose stay in the tropics averaged six months, were examined. Simple methods had of necessity to be used; weight changes, blood-pressure, pulse-rate, cardiovascular response to tilting, and Harvard pack test [3] scores were recorded. A man's efficiency was also assessed by getting his own opinion of how tropical service affected him, and by comparing his views with those of others in a position to judge his work—e.g., his medical officer, commanding officer, and N.C.O. The physical measurements showed no significant changes when compared with those of a control group; but the Harvard pack test score declined steadily with length of service in the tropics. The test consists in stepping on and off a stool every two seconds for five minutes, wearing a pack of one-third the body-weight. Scoring is based on changes in the heart-rate after stopping the exercise. The fall in the scores was slight, but it was correlated significantly with the duration of tropical service. Quite apart from this finding, Macpherson concluded from the subjective and objective assessments of personal efficiency that deterioration was general. Those in the tropical areas agreed, almost universally, that they were less efficient and that they felt less fit. As the physiological measurements showed no changes to explain this decline, it was thought to be largely due to psychological factors.

Ellis, who has published several studies on the effect of environment in the Royal Navy,[4] describes on another page of this issue his work on tropical fatigue in the Navy. His findings are very similar to those of Macpherson, for 80% of those serving in ships in tropical waters considered that they were less efficient than in temperate climates.

The position is still obscure: tropical fatigue may be entirely "subjective," but there can be little doubt of the belief in its existence. It is important to know more about the condition because it affects the whole way of life of the white man in the tropics. Macpherson, for example, attacks the siesta: "One of the cardinal rules for successful tropical living can be summed up in the sentence: keep off your back during daylight hours!" Moreover the social significance of the long-term effects of tropical climates is great, for these have a bearing on emigration policy and on the development of primitive tropical zones. It would be interesting to know whether the native population suffers from tropical fatigue. Ladell [5] has shown that there is no clear difference in acclimatisation to heat between Europeans and Africans in Nigeria; this confirms observations by Weiner [6] on Bantu mine-workers. On the other hand, Robinson et al. found that, among share-croppers in the Southern United States, the Negro workers were mechanically the most efficient; they concluded that the Negroes had a better temperature-regulating mechanism.[7 8]

One of the main difficulties of the subject is the lack of adequate methods of measuring fatigue. Forbes,[9] in his summary of the work of the Harvard Fatigue Laboratory, emphasised this obstacle. When many observers agree that an effect is to be found, it probably exists. Failure to demonstrate the effect quantitatively usually means that the right parameter has not been measured.

CORTISONE VERSUS SALICYLATES

THE striking biological effects of cortisone and A.C.T.H. are echoed, somewhat faintly, by the action of salicylates in heavy doses. In the clinical field the most obvious similarity is the antirheumatic action; and the reported development of Cushing's syndrome in a patient with rheumatic fever receiving 5 g. of aspirin a day [10] stimulated Hetzel and Hine [11] to investigate the effect of salicylates on the pituitary and adrenal glands of rats, using ascorbic-acid depletion as a measure of adrenal cortical response. They showed that sodium salicylate, in doses giving plasma-levels of 15–30 mg. per 100 ml., depleted the adrenal ascorbic acid to an extent related in linear manner to the dose, and that this effect was abolished by hypophysectomy; they also adduced evidence that the salicylate ion acted specifically in this respect, and they concluded that the therapeutic action of salicylates is mediated through the pituitary and adrenal glands. This view is supported by the inhibition of experimental serum arteritis by both cortisone [12 13] and salicylates,[14 15] and by the action of salicylates in increasing urinary output of 17-ketosteroids,[16] in increasing uric acid excretion [17] and in modifying the reversed passive Arthus reaction.[18]

Investigations of the effects of salicylates on the circulating eosinophils, however, have given conflicting results; for while Kelemen et al.[19] and Roskam et al.[20] found eosinopenia after administration of salicylate, Meade and Smith [21] demonstrated no such effect. These workers, moreover, have confirmed [22] Ingle's [23] finding that aspirin causes reduction of glycosuria in diabetic rats, whereas cortisone exacerbates the diabetes; and they challenge the general conclusion of Hetzel and Hine. Lately, Smith [24] has shown that while administration of cortisone to rats on a high carbohydrate diet leads to hyperglycæmia and glycosuria, this effect is much reduced

1. Lee, D. H. K., Macpherson, R. K. *J. appl. Physiol.* 1948, **1**, 60.
2. Macpherson, R. K. *Univ. Qd Pap.* 1949, **1**, no. 10.
3. Harvard Fatigue Laboratory, National Research Council, Division of Medical Science; report no. 8, 1942.
4. Ellis, F. P. Rep. 45/202 to M.R.C. Committee, 1945; *Brit. med. J.* 1948, **1**, 587.
5. Ladell, W. S. S. *J. Physiol.* 1950, **112**, 15P.
6. Weiner, J. S. *Brit. J. industr. Med.* 1950, **7**, 17.
7. Robinson, S., Dill, D. B., Wilson, J. W., Nielsen, M. *Amer. J. trop. Med.* 1941, **21**, 261.
8. Robinson, S., Dill, D. B., Harman, P. M., Hall, F. G., Wilson, J. W. *Hum. Biol.* 1941, **13**, 139.
9. Forbes, W. H. *Psychosom. Med.* 1943, **5**, 155.
10. Cochran, J. B., Watson, R. D., Reid, J. *Brit. med. J.* 1950, ii, 1411.
11. Hetzel, B. S., Hine, D. C. *Lancet*, 1951, ii, 94.
12. Rich, A. R., Berthrong, M., Bennett, I. L. *Bull. Johns Hopk. Hosp.* 1950, **87**, 549.
13. Seifter, J., Ehrich, W. E., Begany, A. J., Warren, G. H. *Proc. Soc. exp. Biol., N.Y.* 1950, **75**, 337.
14. MacGregor, A. G., Wood, D. *Brit. J. Pharmacol.* 1950, **5**, 9.
15. Sullivan, C. J., Parker, T. W., Hibbert, R. W. *Proc. Soc. exp. Biol., N.Y.* 1948, **67**, 508.
16. Bertolani, F., Lorenzini, R., Bonati, B. *Lancet*, 1951, i, 54.
17. Goodman, L., Gilman, A. Pharmacological Basis of Therapeutics. London, 1941; p. 227.
18. Humphrey, J. H. *Brit. J. exp. Path.* 1951, **32**, 274.
19. Kelemen, E., Majoros, M., Ivanyi, J., Kovacs, K. *Experientia*, 1950, **6**, 435. Kelemen, E., Majoros, M. *Lancet*, 1951, i, 926.
20. Roskam, J., Van Cauwenberge, H., Mutsers, A. *Lancet*, 1951, ii, 375.
21. Meade, B. W., Smith, M. J. H. *Ibid*, i, 773.
22. Smith, M. J. H., Meade, B. W., Bornstein, J. *Biochem. J.* 1952, **51**, 18.
23. Ingle, D. J. *Proc. Soc. exp. Biol., N.Y.* 1950, **75**, 673.
24. Smith, M. J. H. *Nature, Lond.* 1952, **170**, 240.

by simultaneous administration of sodium salicylate. In adrenalectomised rats cortisone produced a significant deposition of liver glycogen, but salicylates given in the presence of cortisone caused a contrary and significant depletion. There is, therefore, considerable evidence that the mimicry by salicylates of hormone effects is only partial, and that in experimental conditions salicylates may antagonise cortisone.

In claiming that the therapeutic action of salicylates is mediated through the pituitary, Hetzel and Hine point out that, according to Sayers,[25] a lowered blood-level of cortical hormone stimulates the pituitary to restore homœostasis, and they tentatively suggest that salicylates stimulate the pituitary in this way by increasing the utilisation of cortical hormone in the tissues. In support of this they report experimental evidence that preliminary treatment with cortisone abolishes the ascorbic-acid-depleting effect of salicylates on the adrenals. Conceivably, however, this is a further example of the antagonism between cortisone and salicylates.

THERMOMETERS

DOCTORS learn early that the clinical thermometer is a chancy little tool. If it is to register accurately it must be kept in the mouth for at least three, and in some circumstances, six or seven minutes. Indeed, some years ago in a correspondence on this subject initiated by Dr. Douglas McClean[26] one writer assured us that "ten-minute thermometry has long been the custom in the more efficient sanatoria,"[27] and Dr. E. L. Middleton[28] reported that he always replaced the thermometer in the patient's mouth after the first reading, and went on replacing it after successive readings until two consecutive readings were the same. With these precautions in mind doctors can use thermometers successfully as a guide to one aspect of a case. The general public, however, and even the nursing profession, are not so well trained in scepticism.

Thermometers are made with different sizes of bulb, the smallest being described by manufacturers as "$\frac{1}{2}$ min.," and larger sizes as "1 min." and "2 min." thermometers. These terms were intended to indicate the time the thermometer required to register the true temperature; but the manufacturers know as well as the doctors that the time taken is very variable, depending not merely on the size of the thermometer but on whether it has been kept in a cool or a warm place before use, whether the patient's temperature is high or subnormal, whether he has kept his mouth shut or has had it open for talking, and whether the thermometer is competently placed inside it. Thus it has long been desirable that descriptions by time of different types of thermometer should be given up. The British Standards Institution are now revising the specifications for clinical thermometers. They have never allowed any "time" designation to be stamped on British Standard clinical thermometers, but unfortunately they are now proposing to perpetuate this misleading usage as a trade term. Their reasons for doing so are exactly the same as those given in our columns, in 1943, by Messrs. G. H. Zeal Ltd.,[29] manufacturers of thermometers.

> "Unfortunately," this firm wrote then, "long-standing trade usage and the fact that clinical thermometers have always been sold to the medical profession and the general public as 2 min., 1 min., or $\frac{1}{2}$ min. patterns stand in the way of any change; and while this system of marking is admittedly misleading it has served to differentiate between slow, medium and rapid registering varieties. . . ."

The British Standards Institution, though also admitting that time designations can be (in their own words) "extremely misleading," are nevertheless proposing in their draft that the terms "$\frac{1}{2}$ min. pattern" and "1 min. pattern" should be retained, the inverted commas and the word "pattern" being added, they say, "to show that these designations are, so to speak, trade terms, and are not to be taken as specifying the time required for the thermometer to register correctly." But the housewife, offered the choice of the two "patterns" by a chemist, will have no chance of seeing the inverted commas, and no means of knowing that she is hearing a trade term. She will take a "$\frac{1}{2}$ min. pattern" in good faith, believing she need only keep it in her child's mouth for half a minute to get a reliable reading. The public should not be misled merely because the manufacturers have contracted a bad habit and are unwilling to give it up.

The Association of Scientific Workers, in a comment on the British Standards Institution draft, suggest that the terms "rapid," "medium," and "slow" should be substituted for the misleading terms "$\frac{1}{2}$ min.," "1 min.," and "2 min."; but there are obvious trade objections to marketing a thermometer described as "slow." Moreover, the B.S.I. draft specifies only the "$\frac{1}{2}$ min. pattern," the "1 min. pattern," and the "stubby-bulb pattern"; which suggests that the "2 min. pattern" is no longer on the market. Perhaps appropriate names for the two remaining types would be "long-bulb rapid" and "long-bulb medium" (to distinguish them from the "stubby-bulb pattern"). The A.S.W. make an alternative suggestion—that there should be only one standard clinical thermometer, and that it should have a minimum reading-time of 3 min. stamped on it, with a recommendation that this time should, if possible, be exceeded. Perhaps the device "3 min.+" would suffice. Certainly the public have been trained so consistently to believe that an accurate reading can be taken in half a minute that this piece of re-education is thoroughly necessary.

NEW RELAXANTS

RELAXANTS are nowadays an essential part of anæsthesia. There are a very large number of drugs that interfere with neuromuscular transmission; indeed, pharmacological chemists would probably have little difficulty in synthesising many more of them, for a great deal is known of the relation between chemical structure and relaxant action. The difficulty is to select compounds that will be useful in clinical practice and to assess their value. Studies on animals help greatly; but, because of species difference and the very considerable environmental differences between the pharmacological laboratory and the operating-theatre, the ultimate test must be on patients undergoing an operation.

So far, relaxants seem to be of two main groups. Those in the first group resemble in action the alkaloid *d*-tubocurarine, interfering with the depolarising action of acetylcholine. The others, acting like hexamethonium, cause persistent depolarisation, inhibiting the activity of the neuromuscular junction.

With regard to *d*-tubocurarine, the original relaxant in anæsthesia, there seems to be little real cause for dissatisfaction, though it is generally believed to cause increased oozing owing either to its histaminic effect or to ganglionic block. Its main action persists for about half an hour; this may sometimes be too long, but neostigmine will cut the time short. Of the curare-like relaxants, only gallamine has so far proved a satisfactory substitute for the natural alkaloid. Gallamine is cheaply made and presumably will always be readily obtainable —which tubocurarine may not be. To its discredit it quite often gives rise to tachycardia owing to a vagolytic action.

Of the depolarising group, hexamethonium had a brief period of popularity. It is potent and has a fairly short-

25. Sayers, G. *Physiol. Rev.* 1950, **30**, 241.
26. *Lancet*, 1943, **i**, 446.
27. *Ibid*, p. 539.
28. *Ibid*, p. 725.
29. *Ibid*, p. 510.

lived action, and it was said to be antagonised by pentamethonium. Unfortunately, however, in clinical practice this antagonism cannot be relied on. Nearly a year ago a newcomer to this group, succinylcholine, was introduced. It was reputed to be the safest of all relaxants because of its very short action and rapid disintegration, and the absence of after-effects. Here again early hopes have not been completely fulfilled; for lately there have been many reports of unexpectedly long-continued effects from this "short-acting" relaxant. The criticism that such untoward effects were largely due to overdosage has not wholly stilled uneasiness about the safety of this drug. The latest synthetic relaxant to be tested, known as Compound 20 or 'Laudolissin,' is described in this issue by Dr. Bodman and his colleagues, who report that it acts in a true curare-like manner, is antagonised by neostigmine, lasts a little longer than the natural alkaloid, and apparently has no side-effects. This objective and encouraging report will no doubt stimulate other clinical research-workers to study this drug further.

There is perhaps a danger that successful preliminary tests such as these, made by skilled workers, will be taken by anæsthetists in general as evidence that the drug investigated is the best. That this is not necessarily so is suggested by the story of other relaxants. The somewhat disastrous effect of pentamethonium given to "neutralise" hexamethonium, the unexpected and alarming complications from the use of mephenesin, and the sometimes far from short action of succinylcholine, suggest a need for caution and an open mind.

THE SHAPE OF THE CHEST

COMMUNICATION between humans might be much improved by a collective inward eye. A mental image of a face, a scene, or a patient's physical signs can be so vivid that we itch to pass it on entire. But since visual memories are as subject as other memories to erasions, distortions, and decorations, it is perhaps as well that we rely, for scientific purposes, on less subjective records. The trouble is that some visual images are curiously awkward to record; and among these the shape of the chest ranks high. Dr. H. R. E. Wallis,[1] who has had trouble with it, points out that a photograph does not readily lend itself to accurate measurement; and though funnel chests are fairly easily shown by the camera, Harrison's grooves, to be demonstrated successfully, need a highly skilled photographer. When the subject is a child aged three or four he may also have to be a combination of naturalist, psychologist, and acrobat. Radiography, of course, will show localised deformities of the ribs or spine, and the inclination and spacing of ribs in emphysema and collapse; and lateral views show pigeon and funnel chests. Casts of the chest are useful for following the development of abnormal shapes, such as the bulges associated with congenital heart-disease; but casts are expensive to make and difficult to store, and young children are frightened by the long process of their construction. Even the old-fashioned tape-measure is defeated by this oddly shaped part of the body, this "irregular frustum which ceaselessly expands and contracts in several directions."

Callipers will measure diameters of the chest, and the amount of anteroposterior and lateral respiratory expansion; but since, in children, the expansion is small and the errors in reading apt to be large, the measurements are not of great value. The depth of Harrison's grooves or of a funnel-shaped depression can be measured by a small sliding ruler, attached at right angles to a bar; the bar is laid across the groove, and the ruler pushed in until it touches the bottom of the crater. This measurement, however, tells nothing about the width or slope of the groove: to record these a cyrtometer is needed.

1. *Brit. J. Tuberc.* 1952, 46, 136.

Cyrtometers measure curves, and there are several kinds of them. Strips of soft lead are commonly used, which can be moulded round the chest wall and then removed to a sheet of paper, on which the curves can be traced with a pencil. The two sides of the chest may then be easily compared by superimposing the drawings; and tracings can also be made of the vertical contours of depressions and prominences. Lead, however, is rather stiff, and the physician may find the ribs of a pliable young child fitting themselves to the lead rather than the other way about. Moreover the method is tedious and dirty, and exposes the operator, Dr. Wallis suspects, to a new occupational hazard—chest-physician's colic. He has therefore devised a multiple-rod cyrtometer, composed with great ingenuity from two ebonite plates, 14 in. long and 3 in. wide, and 13 dozen aluminium rods, 9 in. long and $^1/_{16}$ in. in diameter, obtained from the manufacturers of a well-known children's building-set. The lower plate is grooved transversely, and the rods lie side by side in the grooves, projecting on either side of the plate. On top of them is a strip of 'Sorbo' rubber, and then the upper plate; and the plates are held together by two nuts and bolts which allow the rods to be made loose or firm. In practice the rods are loosened, and their free ends are pushed gently against the front of the chest just below the nipple line; they adapt themselves to the shape of the chest wall, forming a line shaped to its contours. The plates are then screwed together, and the outline of the chest wall is traced on paper by running a pencil along the tips of the rods. This little instrument, Dr. Wallis remarks, is easy and quick to use, does not seem to frighten children, and comes in handy when cutting linoleum to fit against moulded corners.

Even an outline of the chest wall, however, does not call up a very lively mental picture of a child's chest. The posture-recorder, used as an aid to physical training in schools, contributes something more.

This consists of a movable lens, a mirror, and a ground-glass screen contained in a box with a flap which acts as a screen against the light. The child stands against a white background, and an image of him in profile is thrown on the glass screen, as in a reflex camera; the outline of this image is traced off on tracing-paper. The method gives a very clear idea of habitual stance, and if the child is shown the tracings they often encourage him to stand better. But small children find it hard to keep still long enough to be drawn, and defective draughtsmanship can influence the result.

Pursuing his ideal of the perfect record, Dr. Wallis has also made use of the optical contour apparatus, designed to facilitate the carving of portrait heads in wood.

It consists of two lamps, each containing two 'Photoflood' bulbs and a parabolic reflector. The lamps are placed opposite each other a foot or so apart, and the light from each of them passes through a screen of plywood strips, $^1/_4$ in. wide and $^1/_{32}$ in. apart. There are 48 strips and 47 spaces; and when anyone stands between the two lighted lamps he is striped with light and dark bands like a zebra. The stripes, of course, follow the contours of his body, and demonstrate very strikingly not only its curves and hollows but any asymmetry between the two sides.

Photographs of children illuminated in this way record accurately the shape of the chest and its movement with respiration; and Dr. Wallis suggests that the apparatus could also be used to record the movements of individual ribs in health and disease.

THE European Congress of Cardiology, which is meeting in London this week, held its first session on Sept. 10. After Sir JOHN PARKINSON, the chairman, had welcomed the delegates, Prof. CHARLES LAUBRY (Paris), the honorary president, delivered his inaugural address. Prof. GUSTAV NYLIN (Stockholm), the president, also spoke.

THE INDEX and title-page to Vol I, 1952, which was completed with THE LANCET of June 28, is now in preparation. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Special Articles

HOT-CLIMATE FATIGUE IN THE ROYAL NAVY

A REVIEW OF LAY OPINION

F. P. ELLIS

O.B.E., M.D. Manc., M.R.C.P.

SURGEON COMMANDER, ROYAL NAVY; DIRECTOR, MEDICAL RESEARCH COUNCIL'S ROYAL NAVAL TROPICAL RESEARCH UNIT, UNIVERSITY OF MALAYA, SINGAPORE

OPINIONS vary concerning the relative importance of the climate as a cause of the increased mental inertia and reduced mental stability which affect some persons who come to the tropics from more temperate zones. When mental breakdown occurs, psychiatrists often find that the hot climate is a less important factor than family separations, failure to readjust to new domestic and social circumstances, economic worries, and over-indulgence in alcohol; but they derive this information from the histories of persons who have already succumbed to the circumstances of their tropical environment—the less robust personalities, the overworked, the convalescent, the unhappily married, and the misfits.

The only way to discover how healthy people react is to ask them, and it is desirable to choose persons who are able to relate their tropical experience to previous experience in a temperate climate. Naval officers and men are appropriate subjects for such an investigation. They are usually selected at random to come to the tropics from a temperate zone. Apart from the difference in climate the other environmental stresses of life in a ship are not very different from those experienced in the Home Fleet and are common to all. Moreover, as the thermal environment between decks is considerably warmer than in residences or offices on shore, the effects of different levels of warmth can also be studied.

Naval opinion on these matters was obtained by means of a voluntary questionnaire distributed in March, 1950, to officers and senior ratings in an aircraft-repair ship who had been serving in tropical waters for six months. The replies were sufficiently interesting to justify the distribution of the same questionnaire to men in a cruiser who had been serving on the East Indies Station for twenty months. It was then circulated to those officers and senior ratings on the staffs of the Commander-in-Chief of the Far East Station, of the Flag Officer of the Malayan Area, and of the Royal Naval Barracks, Singapore, who had been living on shore in the tropics for more than six months.

METHOD

The questionnaire used in each of these investigations is shown in table I. The design enabled those questioned to say whether, in their opinion, they were more or less efficient or more or less healthy in the tropics than in a temperate climate, and to indicate the character of any deterioration they recognised. Leading questions, such as "Have you lost or gained weight?" were avoided. The aim was to identify the features which were most prominent in the mind of the healthy layman without professional prompting. The descriptions of ill health, or of the ways in which efficiency deteriorated, were not necessarily those to which a clinician would attach most emphasis after a careful interview, but they were the features which were most obvious to the men who reported them.

Because of the many differences between naval life on shore and afloat, it was undesirable to compare experiences at sea in the tropics with shore life in a temperate climate. Questions 1 and 4 were designed so that the effects of climate experienced on shore in the tropics could be related to earlier experiences on shore in England, and so that the effects of climate afloat in the tropics could be compared with the effects experienced by the same persons afloat in home waters or in the Mediterranean.

The replies to questions 3 and 5 were sorted together to avoid reduplication when loss of efficiency and loss of health were attributed to the same symptom. The factors to which tropical deterioration was attributed were divisible into those which contributed directly, and others which contributed indirectly, to loss of efficiency. The latter were subdivided into adverse effects associated with excessive sweating and adverse effects not obviously associated with excessive sweating.

RESULTS

About 70 voluntary replies were obtained from each of the ships and from the Singapore establishments. Half of the replies from the aircraft-repair ship and two-thirds from Singapore were from officers, and the rest were from senior ratings. The replies from the cruiser were mostly from ratings (93%), including some junior ratings. In this respect the groups are not strictly comparable.

Reduced Efficiency

Of the men who replied from the ships, 88% thought they were less efficient in the tropics than when serving afloat in a temperate climate (table II); and two-thirds of those who were living on shore held the same opinion. The views of officers and ratings, and of men in different age-groups, were in good agreement.

Impaired Health

In the two ships 72% of the men thought they were less healthy than thay had been when serving in the Home Fleet or the Mediterranean (table III). Several considered

TABLE I—THE QUESTIONNAIRE

CLIMATE AND EFFICIENCY QUESTIONNAIRE

1. Do you consider you are more efficient or less efficient serving afloat on the Far East Station ("afloat on the East Indies Station," "on shore in Singapore") than you were when serving afloat
   (*a*) * in the Home Fleet?..... (*b*) in the Mediterranean? ..... or (*c*) when living on shore in England?.....
2. If you consider you are less efficient in the tropics, do you consider this to be mainly due to the effects of the climate and temperature conditions between decks (climate), or do you consider it to be due to other domestic, economic, or related factors with which this questionnaire is not concerned (other factors)?** .....
3. If you consider that your efficiency is impaired on this station because of the effects of climate, can you give 3 examples of the ways in which you consider the prevailing climatic conditions affect your efficiency adversely?
   (*a*)
   (*b*)
   (*c*)
4. Do you consider you are more healthy or less healthy serving afloat on the Far East Station ("afloat on the East Indies Station," "on shore in Singapore") than you were when serving afloat
   (*a*) in the Home Fleet?..... (*b*) in the Mediterranean? ..... or (*c*) when living on shore in England?.....
5. If you consider you are less healthy on the Far East Station ("East Indies Station," "in Singapore") than you were previously, will you indicate in broad terms the general nature of your decline in health:
6. What is your age?.....
7. Are you married?.....
8. How long have you been in H.M.S..... (stationed in the tropics this commission)?
9. Remarks (please enter on back of form).

Signed:

* Insert "more efficient" or "less efficient," or N.A. (not applicable) if you have served on only one or neither of these stations as appropriate.

** Insert "climate" or "other factors" as appropriate.

Annotations

TROPICAL FATIGUE

In the past the danger of tropical diseases was sufficient reason for Europeans to be advised to avoid long periods in the tropics. The gradual conquest of these diseases has largely removed this danger, but there is still a widespread belief that life in the tropics can lead to physical deterioration. The term "tropical fatigue" has been introduced to describe a decline in efficiency attributable to environmental conditions. The nature of this failure has often been discussed, but there has been little systematic study. During the war, however, tropical fatigue assumed considerable importance, especially in the Pacific area, and an investigation was carried out in the Australian and New Zealand Armed Forces; Lee and Macpherson have given a detailed account of this work.[1 2] The first question that needed answering was: Does tropical fatigue exist? And the second: If it does, is it essentially physiological or psychological?

The investigations were carried out in the field in New Guinea and the adjacent islands. Some 1800 men, whose stay in the tropics averaged six months, were examined. Simple methods had of necessity to be used; weight changes, blood-pressure, pulse-rate, cardiovascular response to tilting, and Harvard pack test [3] scores were recorded. A man's efficiency was also assessed by getting his own opinion of how tropical service affected him, and by comparing his views with those of others in a position to judge his work—e.g., his medical officer, commanding officer, and N.C.O. The physical measurements showed no significant changes when compared with those of a control group; but the Harvard pack test score declined steadily with length of service in the tropics. The test consists in stepping on and off a stool every two seconds for five minutes, wearing a pack of one-third the body-weight. Scoring is based on changes in the heart-rate after stopping the exercise. The fall in the scores was slight, but it was correlated significantly with the duration of tropical service. Quite apart from this finding, Macpherson concluded from the subjective and objective assessments of personal efficiency that deterioration was general. Those in the tropical areas agreed, almost universally, that they were less efficient and that they felt less fit. As the physiological measurements showed no changes to explain this decline, it was thought to be largely due to psychological factors.

Ellis, who has published several studies on the effect of environment in the Royal Navy,[4] describes on another page of this issue his work on tropical fatigue in the Navy. His findings are very similar to those of Macpherson, for 80% of those serving in ships in tropical waters considered that they were less efficient than in temperate climates.

The position is still obscure: tropical fatigue may be entirely "subjective," but there can be little doubt of the belief in its existence. It is important to know more about the condition because it affects the whole way of life of the white man in the tropics. Macpherson, for example, attacks the siesta: "One of the cardinal rules for successful tropical living can be summed up in the sentence: keep off your back during daylight hours!" Moreover the social significance of the long-term effects of tropical climates is great, for these have a bearing on emigration policy and on the development of primitive tropical zones. It would be interesting to know whether the native population suffers from tropical fatigue. Ladell [5] has shown that there is no clear difference in acclimatisation to heat between Europeans and Africans in Nigeria; this confirms observations by Weiner [6] on Bantu mine-workers. On the other hand, Robinson et al. found that, among share-croppers in the Southern United States, the Negro workers were mechanically the most efficient; they concluded that the Negroes had a better temperature-regulating mechanism.[7 8]

One of the main difficulties of the subject is the lack of adequate methods of measuring fatigue. Forbes,[9] in his summary of the work of the Harvard Fatigue Laboratory, emphasised this obstacle. When many observers agree that an effect is to be found, it probably exists. Failure to demonstrate the effect quantitatively usually means that the right parameter has not been measured.

CORTISONE VERSUS SALICYLATES

The striking biological effects of cortisone and A.C.T.H. are echoed, somewhat faintly, by the action of salicylates in heavy doses. In the clinical field the most obvious similarity is the antirheumatic action; and the reported development of Cushing's syndrome in a patient with rheumatic fever receiving 5 g. of aspirin a day [10] stimulated Hetzel and Hine [11] to investigate the effect of salicylates on the pituitary and adrenal glands of rats, using ascorbic-acid depletion as a measure of adrenal cortical response. They showed that sodium salicylate, in doses giving plasma-levels of 15–30 mg. per 100 ml., depleted the adrenal ascorbic acid to an extent related in linear manner to the dose, and that this effect was abolished by hypophysectomy; they also adduced evidence that the salicylate ion acted specifically in this respect, and they concluded that the therapeutic action of salicylates is mediated through the pituitary and adrenal glands. This view is supported by the inhibition of experimental serum arteritis by both cortisone [12 13] and salicylates,[14 15] and by the action of salicylates in increasing urinary output of 17-ketosteroids,[16] in increasing uric acid excretion [17] and in modifying the reversed passive Arthus reaction.[18]

Investigations of the effects of salicylates on the circulating eosinophils, however, have given conflicting results; for while Kelemen et al.[19] and Roskam et al.[20] found eosinopenia after administration of salicylate, Meade and Smith [21] demonstrated no such effect. These workers, moreover, have confirmed [22] Ingle's [23] finding that aspirin causes reduction of glycosuria in diabetic rats, whereas cortisone exacerbates the diabetes; and they challenge the general conclusion of Hetzel and Hine. Lately, Smith [24] has shown that while administration of cortisone to rats on a high carbohydrate diet leads to hyperglycæmia and glycosuria, this effect is much reduced

1. Lee, D. H. K., Macpherson, R. K. *J. appl. Physiol.* 1948, **1**, 60.
2. Macpherson, R. K. *Univ. Qd Pap.* 1949, **1**, no. 10.
3. Harvard Fatigue Laboratory, National Research Council, Division of Medical Science: report no. 8, 1942.
4. Ellis, F. P. Rep. 45/202 to M.R.C. Committee, 1945; *Brit. med. J.* 1948, **i**, 587.
5. Ladell, W. S. S. *J. Physiol.* 1950, **112**, 15P.
6. Weiner, J. S. *Brit. J. industr. Med.* 1950, **7**, 17.
7. Robinson, S., Dill, D. B., Wilson, J. W., Nielsen, M. *Amer. J. trop. Med.* 1941, **21**, 261.
8. Robinson, S., Dill, D. B., Harman, P. M., Hall, F. G., Wilson, J. W. *Hum. Biol.* 1941, **13**, 139.
9. Forbes, W. H. *Psychosom. Med.* 1943, **5**, 155.
10. Cochran, J. B., Watson, R. D., Reid, J. *Brit. med. J.* 1950, **ii**, 1411.
11. Hetzel, B. S., Hine, D. C. *Lancet*, 1951, **ii**, 94.
12. Rich, A. R., Berthrong, M., Bennett, I. L. *Bull. Johns Hopk. Hosp.* 1950, **87**, 549.
13. Seifter, J., Ehrich, W. E., Begany, A. J., Warren, G. H. *Proc. Soc. exp. Biol., N.Y.* 1950, **75**, 337.
14. MacGregor, A. G., Wood, D. *Brit. J. Pharmacol.* 1950, **5**, 9.
15. Sullivan, C. J., Parker, T. W., Hibbert, R. W. *Proc. Soc. exp. Biol., N.Y.* 1948, **67**, 508.
16. Bertolani, F., Lorenzini, R., Bonati, B. *Lancet*, 1951, **i**, 54.
17. Goodman, L., Gilman, A. Pharmacological Basis of Therapeutics. London, 1941; p. 227.
18. Humphrey, J. H. *Brit. J. exp. Path.* 1951, **32**, 274.
19. Kelemen, E., Majoros, M., Ivanyi, J., Kovacs, K. *Experientia*, 1950, **6**, 435. Kelemen, E., Majoros, M. *Lancet*, 1951, **i**, 926.
20. Roskam, J., Van Cauwenberge, H., Mutsers, A. *Lancet*, 1951, **ii**, 375.
21. Meade, B. W., Smith, M. J. H. *Ibid*, **i**, 773.
22. Smith, M. J. H., Meade, B. W., Bornstein, J. *Biochem. J.* 1952, **51**, 18.
23. Ingle, D. J. *Proc. Soc. exp. Biol., N.Y.* 1950, **75**, 673.
24. Smith, M. J. H. *Nature, Lond.* 1952, **170**, 240.

by simultaneous administration of sodium salicylate. In adrenalectomised rats cortisone produced a significant deposition of liver glycogen, but salicylates given in the presence of cortisone caused a contrary and significant depletion. There is, therefore, considerable evidence that the mimicry by salicylates of hormone effects is only partial, and that in experimental conditions salicylates may antagonise cortisone.

In claiming that the therapeutic action of salicylates is mediated through the pituitary, Hetzel and Hine point out that, according to Sayers,[25] a lowered blood-level of cortical hormone stimulates the pituitary to restore homœostasis, and they tentatively suggest that salicylates stimulate the pituitary in this way by increasing the utilisation of cortical hormone in the tissues. In support of this they report experimental evidence that preliminary treatment with cortisone abolishes the ascorbic-acid-depleting effect of salicylates on the adrenals. Conceivably, however, this is a further example of the antagonism between cortisone and salicylates.

THERMOMETERS

DOCTORS learn early that the clinical thermometer is a chancy little tool. If it is to register accurately it must be kept in the mouth for at least three, and in some circumstances, six or seven minutes. Indeed, some years ago in a correspondence on this subject initiated by Dr. Douglas McClean[26] one writer assured us that "ten-minute thermometry has long been the custom in the more efficient sanatoria,"[27] and Dr. E. L. Middleton[28] reported that he always replaced the thermometer in the patient's mouth after the first reading, and went on replacing it after successive readings until two consecutive readings were the same. With these precautions in mind doctors can use thermometers successfully as a guide to one aspect of a case. The general public, however, and even the nursing profession, are not so well trained in scepticism.

Thermometers are made with different sizes of bulb, the smallest being described by manufacturers as "$\frac{1}{2}$ min.," and larger sizes as "1 min." and "2 min." thermometers. These terms were intended to indicate the time the thermometer required to register the true temperature; but the manufacturers know as well as the doctors that the time taken is very variable, depending not merely on the size of the thermometer but on whether it has been kept in a cool or a warm place before use, whether the patient's temperature is high or subnormal, whether he has kept his mouth shut or has had it open for talking, and whether the thermometer is competently placed inside it. Thus it has long been desirable that descriptions by time of different types of thermometer should be given up. The British Standards Institution are now revising the specifications for clinical thermometers. They have never allowed any "time" designation to be stamped on British Standard clinical thermometers, but unfortunately they are now proposing to perpetuate this misleading usage as a trade term. Their reasons for doing so are exactly the same as those given in our columns, in 1943, by Messrs. G. H. Zeal Ltd.,[29] manufacturers of thermometers.

> "Unfortunately," this firm wrote then, "long-standing trade usage and the fact that clinical thermometers have always been sold to the medical profession and the general public as 2 min., 1 min., or $\frac{1}{2}$ min. patterns stand in the way of any change; and while this system of marking is admittedly misleading it has served to differentiate between slow, medium and rapid registering varieties. . . ."

The British Standards Institution, though also admitting that time designations can be (in their own words) "extremely misleading," are nevertheless proposing in their draft that the terms "$\frac{1}{2}$ min. pattern" and "1 min. pattern" should be retained, the inverted commas and the word "pattern" being added, they say, "to show that these designations are, so to speak, trade terms, and are not to be taken as specifying the time required for the thermometer to register correctly." But the housewife, offered the choice of the two "patterns" by a chemist, will have no chance of seeing the inverted commas, and no means of knowing that she is hearing a trade term. She will take a "$\frac{1}{2}$ min. pattern" in good faith, believing she need only keep it in her child's mouth for half a minute to get a reliable reading. The public should not be misled merely because the manufacturers have contracted a bad habit and are unwilling to give it up.

The Association of Scientific Workers, in a comment on the British Standards Institution draft, suggest that the terms "rapid," "medium," and "slow" should be substituted for the misleading terms "$\frac{1}{2}$ min.," "1 min.," and "2 min."; but there are obvious trade objections to marketing a thermometer described as "slow." Moreover, the B.S.I. draft specifies only the "$\frac{1}{2}$ min. pattern," the "1 min. pattern," and the "stubby-bulb pattern"; which suggests that the "2 min. pattern" is no longer on the market. Perhaps appropriate names for the two remaining types would be "long-bulb rapid" and "long-bulb medium" (to distinguish them from the "stubby-bulb pattern"). The A.S.W. make an alternative suggestion—that there should be only one standard clinical thermometer, and that it should have a minimum reading-time of 3 min. stamped on it, with a recommendation that this time should, if possible, be exceeded. Perhaps the device "3 min.+" would suffice. Certainly the public have been trained so consistently to believe that an accurate reading can be taken in half a minute that this piece of re-education is thoroughly necessary.

NEW RELAXANTS

RELAXANTS are nowadays an essential part of anæsthesia. There are a very large number of drugs that interfere with neuromuscular transmission; indeed, pharmacological chemists would probably have little difficulty in synthesising many more of them, for a great deal is known of the relation between chemical structure and relaxant action. The difficulty is to select compounds that will be useful in clinical practice and to assess their value. Studies on animals help greatly; but, because of species difference and the very considerable environmental differences between the pharmacological laboratory and the operating-theatre, the ultimate test must be on patients undergoing an operation.

So far, relaxants seem to be of two main groups. Those in the first group resemble in action the alkaloid *d*-tubocurarine, interfering with the depolarising action of acetylcholine. The others, acting like hexamethonium, cause persistent depolarisation, inhibiting the activity of the neuromuscular junction.

With regard to *d*-tubocurarine, the original relaxant in anæsthesia, there seems to be little real cause for dissatisfaction, though it is generally believed to cause increased oozing owing either to its histaminic effect or to ganglionic block. Its main action persists for about half an hour; this may sometimes be too long, but neostigmine will cut the time short. Of the curare-like relaxants, only gallamine has so far proved a satisfactory substitute for the natural alkaloid. Gallamine is cheaply made and presumably will always be readily obtainable—which tubocurarine may not be. To its discredit it quite often gives rise to tachycardia owing to a vagolytic action.

Of the depolarising group, hexamethonium had a brief period of popularity. It is potent and has a fairly short-

25. Sayers, G. *Physiol. Rev.* 1950, **30**, 241.
26. *Lancet*, 1943, **i**, 446.
27. *Ibid*, p. 539.
28. *Ibid*, p. 725.
29. *Ibid*, p. 510.

lived action, and it was said to be antagonised by pentamethonium. Unfortunately, however, in clinical practice this antagonism cannot be relied on. Nearly a year ago a newcomer to this group, succinylcholine, was introduced. It was reputed to be the safest of all relaxants because of its very short action and rapid disintegration, and the absence of after-effects. Here again early hopes have not been completely fulfilled; for lately there have been many reports of unexpectedly long-continued effects from this "short-acting" relaxant. The criticism that such untoward effects were largely due to overdosage has not wholly stilled uneasiness about the safety of this drug. The latest synthetic relaxant to be tested, known as Compound 20 or 'Laudolissin,' is described in this issue by Dr. Bodman and his colleagues, who report that it acts in a true curare-like manner, is antagonised by neostigmine, lasts a little longer than the natural alkaloid, and apparently has no side-effects. This objective and encouraging report will no doubt stimulate other clinical research-workers to study this drug further.

There is perhaps a danger that successful preliminary tests such as these, made by skilled workers, will be taken by anæsthetists in general as evidence that the drug investigated is the best. That this is not necessarily so is suggested by the story of other relaxants. The somewhat disastrous effect of pentamethonium given to "neutralise" hexamethonium, the unexpected and alarming complications from the use of mephenesin, and the sometimes far from short action of succinylcholine, suggest a need for caution and an open mind.

THE SHAPE OF THE CHEST

COMMUNICATION between humans might be much improved by a collective inward eye. A mental image of a face, a scene, or a patient's physical signs can be so vivid that we itch to pass it on entire. But since visual memories are as subject as other memories to erasions, distortions, and decorations, it is perhaps as well that we rely, for scientific purposes, on less subjective records. The trouble is that some visual images are curiously awkward to record; and among these the shape of the chest ranks high. Dr. H. R. E. Wallis,[1] who has had trouble with it, points out that a photograph does not readily lend itself to accurate measurement; and though funnel chests are fairly easily shown by the camera, Harrison's grooves, to be demonstrated successfully, need a highly skilled photographer. When the subject is a child aged three or four he may also have to be a combination of naturalist, psychologist, and acrobat. Radiography, of course, will show localised deformities of the ribs or spine, and the inclination and spacing of ribs in emphysema and collapse; and lateral views show pigeon and funnel chests. Casts of the chest are useful for following the development of abnormal shapes, such as the bulges associated with congenital heart-disease; but casts are expensive to make and difficult to store, and young children are frightened by the long process of their construction. Even the old-fashioned tape-measure is defeated by this oddly shaped part of the body, this "irregular frustum which ceaselessly expands and contracts in several directions."

Callipers will measure diameters of the chest, and the amount of anteroposterior and lateral respiratory expansion; but since, in children, the expansion is small and the errors in reading apt to be large, the measurements are not of great value. The depth of Harrison's grooves or of a funnel-shaped depression can be measured by a small sliding ruler, attached at right angles to a bar; the bar is laid across the groove, and the ruler pushed in until it touches the bottom of the crater. This measurement, however, tells nothing about the width or slope of the groove: to record these a cyrtometer is needed.

1. *Brit. J. Tuberc.* 1952, **46**, 136.

Cyrtometers measure curves, and there are several kinds of them. Strips of soft lead are commonly used, which can be moulded round the chest wall and then removed to a sheet of paper, on which the curves can be traced with a pencil. The two sides of the chest may then be easily compared by superimposing the drawings; and tracings can also be made of the vertical contours of depressions and prominences. Lead, however, is rather stiff, and the physician may find the ribs of a pliable young child fitting themselves to the lead rather than the other way about. Moreover the method is tedious and dirty, and exposes the operator, Dr. Wallis suspects, to a new occupational hazard—chest-physician's colic. He has therefore devised a multiple-rod cyrtometer, composed with great ingenuity from two ebonite plates, 14 in. long and 3 in. wide, and 13 dozen aluminium rods, 9 in. long and $^1/_{13}$ in. in diameter, obtained from the manufacturers of a well-known children's building-set. The lower plate is grooved transversely, and the rods lie side by side in the grooves, projecting on either side of the plate. On top of them is a strip of 'Sorbo' rubber, and then the upper plate; and the plates are held together by two nuts and bolts which allow the rods to be made loose or firm. In practice the rods are loosened, and their free ends are pushed gently against the front of the chest just below the nipple line; they adapt themselves to the shape of the chest wall, forming a line shaped to its contours. The plates are then screwed together, and the outline of the chest wall is traced on paper by running a pencil along the tips of the rods. This little instrument, Dr. Wallis remarks, is easy and quick to use, does not seem to frighten children, and comes in handy when cutting linoleum to fit against moulded corners.

Even an outline of the chest wall, however, does not call up a very lively mental picture of a child's chest. The posture-recorder, used as an aid to physical training in schools, contributes something more.

This consists of a movable lens, a mirror, and a ground-glass screen contained in a box with a flap which acts as a screen against the light. The child stands against a white background, and an image of him in profile is thrown on the glass screen, as in a reflex camera; the outline of this image is traced off on tracing-paper. The method gives a very clear idea of habitual stance, and if the child is shown the tracings they often encourage him to stand better. But small children find it hard to keep still long enough to be drawn, and defective draughtsmanship can influence the result.

Pursuing his ideal of the perfect record, Dr. Wallis has also made use of the optical contour apparatus, designed to facilitate the carving of portrait heads in wood.

It consists of two lamps, each containing two 'Photoflood' bulbs and a parabolic reflector. The lamps are placed opposite each other a foot or so apart, and the light from each of them passes through a screen of plywood strips, $^1/_4$ in. wide and $^1/_{32}$ in. apart. There are 48 strips and 47 spaces; and when anyone stands between the two lighted lamps he is striped with light and dark bands like a zebra. The stripes, of course, follow the contours of his body, and demonstrate very strikingly not only its curves and hollows but any asymmetry between the two sides.

Photographs of children illuminated in this way record accurately the shape of the chest and its movement with respiration; and Dr. Wallis suggests that the apparatus could also be used to record the movements of individual ribs in health and disease.

THE European Congress of Cardiology, which is meeting in London this week, held its first session on Sept. 10. After Sir JOHN PARKINSON, the chairman, had welcomed the delegates, Prof. CHARLES LAUBRY (Paris), the honorary president, delivered his inaugural address. Prof. GUSTAV NYLIN (Stockholm), the president, also spoke.

THE INDEX and title-page to Vol I, 1952, which was completed with THE LANCET of June 28, is now in preparation. A copy will be sent gratis to subscribers on receipt of a postcard addressed to the Manager of THE LANCET, 7, Adam Street, Adelphi, W.C.2. Subscribers who have not already indicated their desire to receive indexes regularly as published should do so now.

Special Articles

HOT-CLIMATE FATIGUE IN THE ROYAL NAVY

A REVIEW OF LAY OPINION

F. P. ELLIS

O.B.E., M.D. Manc., M.R.C.P.

SURGEON COMMANDER, ROYAL NAVY; DIRECTOR, MEDICAL RESEARCH COUNCIL'S ROYAL NAVAL TROPICAL RESEARCH UNIT, UNIVERSITY OF MALAYA, SINGAPORE

OPINIONS vary concerning the relative importance of the climate as a cause of the increased mental inertia and reduced mental stability which affect some persons who come to the tropics from more temperate zones. When mental breakdown occurs, psychiatrists often find that the hot climate is a less important factor than family separations, failure to readjust to new domestic and social circumstances, economic worries, and over-indulgence in alcohol; but they derive this information from the histories of persons who have already succumbed to the circumstances of their tropical environment—the less robust personalities, the overworked, the convalescent, the unhappily married, and the misfits.

The only way to discover how healthy people react is to ask them, and it is desirable to choose persons who are able to relate their tropical experience to previous experience in a temperate climate. Naval officers and men are appropriate subjects for such an investigation. They are usually selected at random to come to the tropics from a temperate zone. Apart from the difference in climate the other environmental stresses of life in a ship are not very different from those experienced in the Home Fleet and are common to all. Moreover, as the thermal environment between decks is considerably warmer than in residences or offices on shore, the effects of different levels of warmth can also be studied.

Naval opinion on these matters was obtained by means of a voluntary questionnaire distributed in March, 1950, to officers and senior ratings in an aircraft-repair ship who had been serving in tropical waters for six months. The replies were sufficiently interesting to justify the distribution of the same questionnaire to men in a cruiser who had been serving on the East Indies Station for twenty months. It was then circulated to those officers and senior ratings on the staffs of the Commander-in-Chief of the Far East Station, of the Flag Officer of the Malayan Area, and of the Royal Naval Barracks, Singapore, who had been living on shore in the tropics for more than six months.

METHOD

The questionnaire used in each of these investigations is shown in table I. The design enabled those questioned to say whether, in their opinion, they were more or less efficient or more or less healthy in the tropics than in a temperate climate, and to indicate the character of any deterioration they recognised. Leading questions, such as "Have you lost or gained weight?" were avoided. The aim was to identify the features which were most prominent in the mind of the healthy layman without professional prompting. The descriptions of ill health, or of the ways in which efficiency deteriorated, were not necessarily those to which a clinician would attach most emphasis after a careful interview, but they were the features which were most obvious to the men who reported them.

Because of the many differences between naval life on shore and afloat, it was undesirable to compare experiences at sea in the tropics with shore life in a temperate climate. Questions 1 and 4 were designed so that the effects of climate experienced on shore in the tropics could be related to earlier experiences on shore in England, and so that the effects of climate afloat in the tropics could be compared with the effects experienced by the same persons afloat in home waters or in the Mediterranean.

The replies to questions 3 and 5 were sorted together to avoid reduplication when loss of efficiency and loss of health were attributed to the same symptom. The factors to which tropical deterioration was attributed were divisible into those which contributed directly, and others which contributed indirectly, to loss of efficiency. The latter were subdivided into adverse effects associated with excessive sweating and adverse effects not obviously associated with excessive sweating.

RESULTS

About 70 voluntary replies were obtained from each of the ships and from the Singapore establishments. Half of the replies from the aircraft-repair ship and two-thirds from Singapore were from officers, and the rest were from senior ratings. The replies from the cruiser were mostly from ratings (93%), including some junior ratings. In this respect the groups are not strictly comparable.

Reduced Efficiency

Of the men who replied from the ships, 88% thought they were less efficient in the tropics than when serving afloat in a temperate climate (table II); and two-thirds of those who were living on shore held the same opinion. The views of officers and ratings, and of men in different age-groups, were in good agreement.

Impaired Health

In the two ships 72% of the men thought they were less healthy than thay had been when serving in the Home Fleet or the Mediterranean (table III). Several considered

TABLE I—THE QUESTIONNAIRE

CLIMATE AND EFFICIENCY QUESTIONNAIRE

1. Do you consider you are more efficient or less efficient serving afloat on the Far East Station ("afloat on the East Indies Station," "on shore in Singapore") than you were when serving afloat
   (*a*) • in the Home Fleet? ..... (*b*) in the Mediterranean? ..... or (*c*) when living on shore in England? .....
2. If you consider you are less efficient in the tropics, do you consider this to be mainly due to the effects of the climate and temperature conditions between decks (climate), or do you consider it to be due to other domestic, economic, or related factors with which this questionnaire is not concerned (other factors)?** .....
3. If you consider that your efficiency is impaired on this station because of the effects of climate, can you give 3 examples of the ways in which you consider the prevailing climatic conditions affect your efficiency adversely?
   (*a*)
   (*b*)
   (*c*)
4. Do you consider you are more healthy or less healthy serving afloat on the Far East Station ("afloat on the East Indies Station," "on shore in Singapore") than you were when serving afloat
   (*a*) in the Home Fleet? ..... (*b*) in the Mediterranean? ..... or (*c*) when living on shore in England? .....
5. If you consider you are less healthy on the Far East Station ("East Indies Station," "in Singapore") than you were previously, will you indicate in broad terms the general nature of your decline in health:
6. What is your age? .....
7. Are you married? .....
8. How long have you been in H.M.S. ..... (stationed in the tropics this commission)?
9. Remarks (please enter on back of form).

Signed:

• Insert "more efficient" or "less efficient," or N.A. (not applicable) if you have served on only one or neither of these stations as appropriate.

•• Insert "climate" or "other factors" as appropriate.

TABLE II—NUMBERS WHO CONSIDERED THEY WERE LESS EFFICIENT IN THE TROPICS THAN IN A COOLER CLIMATE

Age-group (yr.)	Cruiser (20 mos. in tropics)			Repair ship (6 mos. in tropics)			Shore bases in Singapore (more than 6 mos. in tropics)		
	Officers	Ratings	Total	Officers	Ratings	Total	Officers	Ratings	Total
20–29	2/2 (100%)	30/37 (81%)	32/39 (82%)	8/10 (80%)	21/21 (100%)	29/31 (94%)	3/6 (50%)	8/11 (73%)	11/17 (65%)
30–39	2/3 (67%)	17/21 (81%)	19/24 (79%)	9/9 (100%)	11/11 (100%)	20/20 (100%)	13/21 (62%)	11/14 (79%)	24/35 (69%)
40–49	..	..	..	8/9 (89%)	2/2 (100%)	10/11 (91%)	9/13 (69%)	2/3 (67%)	11/16 (69%)
50–59	..	..	..	..	..	..	1/3 (33%)	..	1/3 (33%)
Total	4/5 (80%)	47/58 (81%)	51/63 (81%)	25/28 (89%)	34/34 (100%)	59/62 (95%)	26/43 (60%)	21/28 (75%)	47/71 (66%)
No reply	..	6	6	4	1	5	2	..	2
Numbers questioned	5	64	69	32	35	67	45	28	73

TABLE III—NUMBERS WHO CONSIDERED THEY WERE LESS HEALTHY IN THE TROPICS THAN IN A COOLER CLIMATE

20–29	1/2 (50%)	28/38 (74%)	29/40 (73%)	5/10 (50%)	15/21 (71%)	20/31 (65%)	3/6 (50%)	6/11 (55%)	9/17 (53%)
30–39	2/3 (67%)	17/21 (81%)	19/24 (79%)	6/9 (67%)	10/11 (91%)	16/20 (80%)	5/20 (25%)	5/12 (42%)	10/32 (31%)
40–49	..	..	..	5/9 (56%)	2/2 (100%)	7/11 (64%)	5/13 (38%)	1/3 (33%)	6/16 (38%)
50–59	..	..	..	..	..	..	0/3	..	0/3
Total	3/5 (60%)	45/59 (76%)	48/64 (75%)	16/28 (57%)	27/34 (79%)	43/62 (69%)	13/42 (31%)	12/26 (46%)	25/68 (37%)
No reply	..	5	5	4	1	5	3	2	5
Numbers questioned	5	64	69	32	35	67	45	28	73

that they were more healthy but less efficient in the tropics. On the other hand 63% of those who were living and working on shore thought that their health was as good as, or better than, it had been in a temperate climate.

Direct Causes of Loss of Efficiency

The subjects' descriptions of the ways in which climate affected efficiency are classified in table IV according to the main symptom groups which they suggest.

The frequency with which these features were reported in the two ships and by the shore-based subjects is shown in table V. The outstanding complaint was lethargy or tiredness in some form or other. In the cruiser 51 out of 63 (81%) reported reduced efficiency (table II), and lethargic symptoms were referred to. Memory defects were reported by 78% of those who were questioned (table V). The office workers on shore were more aware of memory defects, and also of slowing of their mental processes, than those in ships, although fewer of them reported lethargic symptoms. Officers and ratings replied in very similar terms, with only a few differences worthy of mention. Whereas five times as many officers as men in the repair ship commented on a lowered sense of responsibility, five times as many ratings as officers reported symptoms indicating retardation. These changes in emphasis were largely due to differences in relative responsibilities and occupations. Responsibilities of the officers were greater than those of the ratings. The ratings included many skilled technicians and mechanics who were more likely to observe retarding effects in their work.

Indirect Causes of Loss of Efficiency

The reported complaints which were probably associated with excessive sweating are summarised in table VI. The men who were living on shore had few complaints other than mild skin disease. In clear contrast about half the replies from ships referred to discomfort, unsatisfactory sleep, and skin diseases, caused or aggravated by unevaporated sweat on the skin or in the clothing or the bedding.

Discomfort was reported in nearly 60% of the replies from the ships but in only 10% of replies from men living on shore. It was referred to in various ways: "excessive perspiration"; "skin irritation due to sweating"; "physical discomfort off duty"; "physical discomfort reduces will to work"; "heat increases the unpleasant effects of overcrowding"; "unable to relax"; "sweat runs in the eyes"; "perspiration interferes with bench work"; "paper work gets covered with sweat"; "perspiration interferes with the playing of string and wind instruments."

Disturbed or inadequate sleep was mentioned by 44% of the men in the ships but by only 4% of those on shore. Typical observations were: "sleep is interrupted"; "too hot to sleep well"; "continuous feeling of lack of sleep"; "more sleep is required"; "wake up feeling tired."

The complaints not obviously associated with sweating are summarised in table VII. The volunteers living on shore had few complaints. After six months in the tropics, however, a proportion of men in the repair ship reported loss of appetite and weight. These features were referred to in nearly 25% of the replies from the cruiser after

TABLE IV—SUBJECTS' DESCRIPTIONS OF WAYS IN WHICH THEIR EFFICIENCY WAS REDUCED

SYMPTOM	SUBJECTS' DESCRIPTION
Lethargy	Lassitude. Lack of energy. Listlessness. Fatigue easily. Less staying-power. Tire quickly. Less stamina. Easily exhausted. Lack of vitality. Lack of alertness. Physical and mental fatigue. Capacity for long hours less. Hard to stay awake, especially in afternoons.
Reduced concentration	Cannot concentrate. Hard to concentrate on intricate jobs. Hard to think profoundly. "Grasshopper mind." Reduced concentration in the afternoons.
Retardation	More effort is required. Think more slowly. Manual work is more difficult. Reactions are slower. Work takes longer. Output of work is less. Inclination to go slower. More difficult to learn new subjects. New problems must be tackled more slowly. Slowing of mental and physical activities. Capacity for work is less.
Lowered responsibility	Tendency to leave or rush work in hot spaces. Neglect of detail. Less incentive to explore responsibilities in hot situations. Procrastination. "Couldn't care less" attitude. Less drive. Accept reports without scrutinising them. Too hot to "jump to it" and "dash around." Tendency to avoid physical effort. Tendency to avoid office work. Make hasty decisions. Lack of interest. Lazy mentally. Harder to maintain discipline. Less keen to get out of the office and see for oneself. Inclined to take the path of least resistance. "Slap-dash" methods.
Personality change	Short-tempered. Irritable. Impatient. Depressed. Neurotic. Anxious. Apathetic. Inclined to worry more. Minor troubles are magnified out of all proportion to their real importance.
Memory defects	Forgetfulness. Forget simple things. Absent-minded. More effort is required to remember.

TABLE V—NUMBERS REPORTING REDUCED EFFICIENCY

—	Cruiser (20 mos. in tropics)	Repair ship (6 mos. in tropics)	Shore bases in Singapore (more than 6 mos. in tropics)
Lethargy	54 (78%)	44 (66%)	31 (42%)
Reduced concentration	14 (20%)	21 (31%)	22 (30%)
Retardation	6 (9%)	14 (21%)	18 (25%)
Lowered sense of responsibility	16 (23%)	23 (34%)	10 (14%)
Personality changes	13 (19%)	22 (33%)	13 (18%)
Memory defects	3 (4%)	5 (7%)	13 (18%)
No. questioned	69	67	73

TABLE VI—NUMBERS REPORTING ADVERSE EFFECTS PROBABLY ASSOCIATED WITH EXCESSIVE SWEATING

Discomfort	38 (55%)	39 (58%)	7 (10%)
Disorders of sleep	31 (45%)	29 (43%)	3 (4%)
Diseases of the epidermis:	34 (49%)	32 (48%)	16 (22%)
Prickly heat	14 (20%)	25 (37%)	5 (7%)
Fungus infections	12 (17%)	4 (6%)	2 (3%)
Cuts go septic or take longer to heal	3 (4%)	8 (12%)	5 (7%)
Scalp affections	2 (3%)	0	0
Ear affections	3 (4%)	1 (1·5%)	0
Boils	3 (4%)	1 (1·5%)	3 (4%)
No. questioned	69	67	73

TABLE VII—NUMBERS REPORTING ADVERSE EFFECTS OF TROPICAL SERVICE NOT OBVIOUSLY ATTRIBUTABLE TO EXCESSIVE SWEATING

Loss of appetite	17 (25%)	9 (13%)	1 (1·4%)
Loss of weight	16 (23%)	4 (6%)	2 (2·7%)
Gastro-intestinal disorders, indigestion, constipation	5 (7%)	9 (13%)	4 (5·5%)
Common cold, respiratory infections	8 (12%)	3 (4%)	4 (5·5%)
Headache	12 (17%)	4 (6%)	2 (2·7%)
General debility	6 (9%)	2 (3%)	1 (1·4%)
No. questioned	69	67	73

twenty months' service on the East Indies Station, and 17% complained of headaches.

The reported loss of weight in the cruiser was supported by a review at random of the weights of 35 members of the ship's company obtained during their PULHEEMS examinations after about six months and eighteen months in the tropics. There was an average weight loss of 1·7 lb. for the group, which was statistically significant. This did not include any initial losses on arrival in the tropics, and was due mainly to losses by those who were above average weight, for 17 men above the average weight of 145 lb. lost 2·8 lb. on the average, which was also significant; whereas the average loss by 18 men below average weight was only 0·66 lb., which was not significant.

Only 2 men referred to dizziness, and only 2 to swollen feet and swollen legs; 7 men (2 in the cruiser, 2 in the repair ship, and 3 on shore) commented on the unpleasant effects of sun glare on the eyes.

Importance of Climate

The great majority (over 80%) of those who thought they were less efficient in the tropics, either on shore or afloat, considered that loss of efficiency was due mainly to climatic factors (table VIII). Only 4 out of 157 men (2·5%) considered that domestic, economic, or related factors were more important than the tropical climate. The remainder thought that climate and other factors were implicated equally.

DISCUSSION

It is of value to see how far these statements of opinion are supported by accounts of war-time experience. The resemblance is close between the picture of "hot-climate" fatigue in these ships and that described as "tropical fatigue" by Macpherson (1949) in the New Guinea area in 1944. The term "hot-climate" fatigue is used here because symptoms attributed directly to the effects of excessive warmth were so prominent, and also because the climate in the tropics is very pleasant for much of the time, particularly at the higher altitudes, and because unpleasantly warm climates are encountered outside the tropics.

Macpherson obtained his information by the examination and systematic interrogation of "fit men" in their units. The majority had only been in the tropics about six months. The characteristic complaints were sleepiness, headaches, vague abdominal pain, loss of appetite, pains in the back, loss of weight, and dizziness on standing up. He devoted special attention to dizziness, and found that this symptom was in fact less common (33/1257, or 2·6%) than the reported incidence of "blackouts" suggested. The incidence of dizziness in the present naval replies was even smaller (2/209, about 1%), probably because the subjects were not questioned directly on this point and because the psychological stresses of war were removed. Macpherson's objective observations, including tests for circulatory instability, reduced ability to carry out a set physical task, and periodic weighing, did not suggest a serious degree of physical deterioration. He concluded that tropical fatigue was partly physical, because ill health, particularly skin disease, was more prominent than in a control series of men not serving in the tropics, but that it was psychological to a very much greater extent. The climatic factor was important in its causation, although isolation, boredom, conditions of service, and the moral fibre of the men had to be considered as well.

In an account of naval psychiatric cases observed at Bombay and Trincomalee, Cameron (1945) gave the clinician's viewpoint. He described first the vague symptoms encountered commonly outside the consulting-room:

> "Lassitude, tiredness and awareness of the temperature . . . a somewhat lowered tempo of performance and the need to accept slightly lowered standards in oneself and others. The effects on work and interests, at first, are not markedly significant, and a good performance and healthy outlook are maintained with two exceptions, immediate memory and capacity for concentration are impaired. . . . A serious consequence of impaired attention and anxiety . . . is irritability."

So far the comparison with the present replies is again close. In a contemporary account Critchley (1945) considered that to a newcomer to the tropics the syndrome of undue irritability, alcoholic indulgence, mild hypochondriacal preoccupation, and a tendency towards paranoid feelings of resentment was suggestive of a mild dementia with personality deterioration—but for the clear insight of those affected and the fact that the condition was cured after leave at home.

TABLE VIII—MEN WHO REPORTED LOSS OF EFFICIENCY TO BE DUE TO CLIMATIC FACTORS, NON-CLIMATIC FACTORS, OR A COMBINATION OF BOTH

—	Cruiser (20 mos. in tropics)			Repair ship (6 mos. in tropics)			Shore bases in Singapore (more than 6 mos. in tropics)		
	Officers	Ratings	Total	Officers	Ratings	Total	Officers	Ratings	Total
Climatic factors	2 (50%)	39 (83%)	41 (80%)	20 (80%)	28 (85%)	48 (83%)	22 (85%)	16 (76%)	38 (81%)
Non-climatic factors	—	—	—	1 (4%)	1 (3%)	2 (3%)	1 (4%)	1 (5%)	2 (4%)
Both	2 (50%)	8 (17%)	10 (20%)	4 (16%)	4 (12%)	8 (14%)	3 (11%)	4 (19%)	7 (15%)
No reply to question 2	—	—	—	—	1	1	—	—	—
Total	4	47	51	25	34	59	26	21	47

Cameron then described a "prepsychotic tropical syndrome" which emerged occasionally from this broad backcloth. This was typified by dullness, apathy, unwillingness to confide, tremulousness, conscious anxiety, and paranoid outlook, but not by failure of the intellectual faculties, disorientation, or hallucinosis. Established psychoses (conditions certifiable by British law) were responsible for 1 in 7 of the total number of patients he interviewed. Nearly all the patients seen at Trincomalee came from ships, and nearly half of them showed physical evidence of an adverse reaction to heat, such as prickly heat or some other form of skin disease, in contrast with only 10% at Bombay, where the majority were based on shore. The history was not usually that of an unstable person. The usual progress was towards recovery though the patient remained in the tropics. The peak incidence occurred among those who had been less than six months or more than eighteen months on the station. An unduly high proportion were men aged more than 40. Marital unhappiness was a factor in 25% of the cases. Cameron probably saw a more severe state of affairs than he would have encountered in peace-time, because of the more strenuous climatic and operational conditions of the war afloat, and the larger numbers of older and conscripted men exposed to these stresses.

The emphasis laid by Cameron (1945) and Critchley (1945) on the importance of psychological deterioration in the tropics was not supported by the monthly returns of sickness from the Eastern and British Pacific Fleets between February, 1944, and August, 1945, when the average monthly incidence of fresh patients reporting for treatment who were diagnosed to be suffering primarily from a psychoneurotic disorder never exceeded 0·1% of those at risk (Ellis 1948). On the other hand, skin diseases, excluding uncomplicated prickly heat, caused 10% of ships' companies to report for treatment each month. It has been suggested that, if you eliminate the psychiatrist, psychiatric illness will not figure largely in routine sickness returns; and psychiatrists were in short supply in the Eastern Fleet. This is not to say that psychiatric complaints ceased to exist but that greater prominence was probably given by those living in ships to coincidental physical complaints.

The incidence of the more common causes of ill health was nearly twice as great in ships as in shore establishments. The time lost by air-crew in a fleet aircraft-carrier because of sickness was three times as great in the tropics during the third quarter of 1944 as in the second quarter of that year when the ship was operating off the Norwegian coast (Rogerson 1945). The average working time lost through sickness in a cruiser and a battle-cruiser during five and eight months respectively in the Eastern Fleet in the same year was nearly thrice that lost in the previous period when these ships were in the Mediterranean (Ellis 1945). In the first year after the war the weekly sickness returns from all ships revealed that total sickness was more than doubled in tropical as contrasted with northern temperate waters, and diseases of the skin were increased by three or four times (Fraser Roberts 1948).

There was little doubt that efficiency was also reduced because of the warmth of the environment between decks, although it was not easy to prove this. Men decoding signals in cypher offices, accountants, store officers, and others engaged in sedentary mental work described how, after short periods in their hot offices, they were unable to think and either felt drowsy, made unreasonable mistakes, or failed to concentrate altogether. Others remarked how mistakes were made often without the knowledge of the person making the mistake. Officers in charge of gunnery-control positions noticed that the crews of transmitting stations and calculating positions made more individual errors and their team-work was not so good as it was in home waters. Engineer officers reported that the work of skilled technicians was of a poorer quality than the work turned out in a cooler climate, and the winding of electrical armatures in electrical repair shops took longer, although more men were occupied on this work. Heavier work, such as "bombing-up" a wing of 24 aircraft in a carrier, took half as long again in the tropics.

Experimental evidence also supports the view that efficiency was reduced. The average effective temperature (Bedford 1946) on the mess-decks in the Eastern Fleet was 84°F, and much warmer conditions were encountered in most places where the crews worked between decks (Ellis 1948). Mackworth (1951), in a series of experiments carried out under controlled climatic conditions at Cambridge, showed that the level of performance of men carrying out tasks simulating those of wireless telegraphy, radar, and gunnery ratings deteriorated when the effective temperature of the climate in which they were working was raised from 81° to 86°F.* Observations made at Singapore by Pepler (1951) on naval ratings acclimatised to the tropics also confirm Mackworth's assumption that the performance of certain tasks will deteriorate with increasing warmth at these climatic levels, although he found rather more variability than Mackworth in the levels of warmth at which these effects were observed.

Hot-climate fatigue, though less obvious, was probably just as common as prickly heat in the Eastern Fleet during the war, and when the latter was rife in a ship's company it was a useful indicator of the presence of the former. Under operational conditions it was the rule rather than the exception in many ships, but it did not lead to serious breakdown very often, as it might have done in a less stable community. A man affected by hot-climate fatigue does not necessarily feel ill; indeed his attitude is at times euphoric rather than gloomy. He is unlikely to call on the doctor because he feels more lethargic, less responsible, more forgetful, or more irritable than he is accustomed to be; nor will he seek in the sick-bay a cure for incessant sweating, for these are accepted as unavoidable concomitants of life in an excessively warm climate. When practically everybody is affected to some extent, such features of abnormality are often accepted as normal within the community, although they may appear strikingly abnormal to a trained observer fresh from a temperate climate (Critchley 1945). These men were fatigued by chronic discomfort from continuous sweating, chronic skin diseases, lack of sleep, salt deficiency in some cases, and the body's never-ending struggle to maintain itself in thermal equilibrium with its environment, added to the cumulative effect of four or five years' vigorous naval warfare. When they obtained relief from their hot living and working conditions they usually recovered quickly. When the occasion demanded it, either in action or for the captain's rounds or other inspections, the very great majority would "snap out of it" for the time being, although between times a relaxation of standards, general appearances, and responsibilities, which could not be conducive to full efficiency, might be accepted without comment. The truth probably lay somewhere between the sorry story told by the few psychiatrists in their overcrowded clinics and the more optimistic statements of executive officers who were impressed by what they saw at inspections or by efficiency in action when men were keyed up to give their best performance.

The thermal environment between decks is much warmer than in offices and barracks on shore. In the tropics the average temperature of the air in the living-spaces, which are the cooler parts of a ship, is about 7°F higher than that of the outside air. At these levels

* The actual environments used by Mackworth were dry-bulb and wet-bulb temperatures of 90/80°F and 95/85°F when the average air movement was about 100 ft./min. and the men were stripped to the waist.

of warmth this makes all the difference between a climate which is tolerable and one which is too warm for comfort (Ellis 1952). Adequate methods for controlling the climate within warships are available today; but the necessary modifications in design must be compatible with the other requirements of a fighting ship, and acceptable in other climates.

SUMMARY

Naval officers and ratings serving afloat and on shore in the tropics answered a questionnaire about the effect of climate on their efficiency and health.

The great majority of those serving in the ships thought that they were less efficient in the tropics than when serving afloat in more temperate waters, and two-thirds of those living on shore thought that they were less efficient than when serving on shore in England. Climatic factors were regarded as the main cause of this loss of efficiency by over 80% of 157 men who thought they were less efficient, and only 4 men (2·5%) considered domestic, economic, or related factors to be more important than climate. The views expressed by officers and men were in close agreement.

Whereas over 70% of those in the ships thought that they were less healthy in the tropics, nearly two-thirds of those living on Singapore Island thought that they were equally healthy or more healthy in the tropics than in a temperate climate.

When healthy men serve for a long time in an unduly warm climate, some of them will suffer from hot-climate fatigue, typified by lethargy, mental retardation, reduced powers of concentration and sense of responsibility, irritability, and mild changes in personality and forgetfulness, which are associated often with excessive sweating, unsatisfactory sleep, skin diseases, loss of weight, loss of appetite, and ill-defined digestive disorders. This syndrome develops when men live and work at levels of warmth which result in the presence of unevaporated sweat on the skin and in the clothing or bedding. The majority of men exposed to these conditions will suffer in one way or another after a time, but in a healthy community serious breakdown will not be encountered very often, and there will be little reference to the condition in routine sickness returns. Most of these effects can be surmounted temporarily when it is necessary to make a special effort, and are relieved by resumption of life in a cooler climate.

The evidence available suggests that hot-climate fatigue does not raise many serious problems among the male naval community in Singapore Island but becomes increasingly prominent with long service afloat in a tropical climate.

This account is published by permission of the Admiralty and the Medical Research Council's Royal Naval Personnel Research Committee. I am indebted to the Commander-in-Chief, Far East Station, and the Flag Officer, Malayan Area, for permission to circulate the questionnaire; to Surgeon Commander T. Barlow, R.N., who arranged for its distribution and collection in the cruiser; to the officers and men who provided the answers; and to Sir Frederic Bartlett, Dr. R. K. Macpherson, Dr. J. O. Irwin, and Dr. K. Cameron for helpful advice.

REFERENCES

Bedford, T. (1946) Environmental Warmth and its Measurement. Medical Research Council War Memorandum no. 17. H.M. Stationery Office.
Cameron, K. (1945) Rep. 45/252 M.R.C. Royal Naval Personnel Research Committee.
Critchley, M. (1945) *Brit. med. J.* ii, 208.
Ellis, F. P. (1945) Rep. 45/202 M.R.C. Royal Naval Personnel Research Committee.
— (1948) *Brit. med. J.* i, 587.
— (1952) *J. Hyg., Camb.* (in the press).
Fraser Roberts, J. A. (1948) *Brit. J. soc. Med.* **2**, 55.
Mackworth, N. H. (1951) *Spec. Rep. Ser. med. Res. Coun., Lond.* no. 268.
Macpherson, R. K. (1949) *Univ. Queensland Papers (Physiol.)* **1**, 1.
Pepler, R. D. (1951) Unpublished rep., M.R.C. Royal Naval Personnel Research Committee.
Rogerson, J. P. G. (1945) Appendix v, rep. 45/202 M.R.C. Royal Naval Personnel Research Committee.

THE HEALTH OF THE ARMY

In the complexities, stresses, and strains of modern warfare, health has become increasingly important to the fighting Services; and the switch of emphasis from the prevention of disease to the attainment and maintenance of health is shown by the change of title of the Directorate of Hygiene to that of Army Health. This tendency can also be seen in the recently published Report on the Health of the Army in the years 1946–48, which covers the period of demobilisation and run-down from the war-time peak.*

HEALTH EDUCATION

An accurate definition of "health" and a satisfactory method of assessing it are essential; and the chapter on recruiting and medical classification is important. The introduction in 1948 of the PULHEEMS system of medical classification into the three Services improved the assessment of physical and mental health; and the Interdepartmental Standing Committee on Medical Classification, set up in the same year, was given the responsibility, among others, of keeping the PULHEEMS system up to date. The lead given by the Services in medical classification and in personnel selection might with advantage be followed in civilian life to a greater extent than at present.

During these post-war years physical training was modified in accordance with the Army's changing requirements. Coöperation between physical-training staffs and the medical services became closer; and medical supervision of the recruit and the trained man in their basic and battle training, and tests, was intensified. The remedial aspect of physical training for the sick and wounded and for the substandard recruit was also developed, especially at the three physical-development centres, where the physique of substandard recruits was built up. In 1946 these three centres were amalgamated in one centre at Chester, accommodating 1800 recruits. In 1948 man-power shortage led, unfortunately, to its closure. Presumably mobilisation plans provide for these centres to be reopened. But it might be worth considering whether these substandard recruits should not be detected long before call-up, and given physical-development courses under civilian auspices before they leave school.

The Army tackled health education vigorously. All cadets and recruits, and all officers, N.C.O.s, and trained men received essential instruction, planned according to their needs, from medical officers, and instructors trained at the Army School of Health. At the school and in centres abroad, courses were held for unit sanitary and water-duty personnel. Instruction on service in the tropics and subtropics was given on all troopships proceeding to the Middle and Far East. All possible use was made of films, filmstrips, models, pamphlets, books, and the like. The difficulty was to ensure that, in the welter of training and instruction which the soldier received, sufficient time was set aside for education in health. In this the support of the military training authorities was invaluable.

ENVIRONMENTAL RESEARCH

During the late war personnel research was carried out under the ægis of the Military Personnel Research Committee, which lapsed in 1945. In 1948, in view of the increasing complexity of modern equipment and of the wide range of environments in which the soldier of today has to serve, a new committee was formed, under the chairmanship of Sir Charles Lovatt-Evans, F.R.S., to consider applied physiological and psychological research. The members include civilian physiologists and psychologists as well as representatives of the three Services and of the Ministry of Supply. Four subcommittees deal

* This report is not on sale, but copies have been sent to learned societies.

with special aspects of the work, such as clothing and equipment, fighting vehicles, and steel helmets and body armour. Some progress has been made, but the personnel and resources for the large amount of applied research required seem inadequate. Fundamental research remains the responsibility of the Medical Research Council through its Interservices Personnel Research Committee.

Of recent years soldiers have been increasingly exposed to industrial hazards owing to the formation of large workshops, light-aid detachments, and similar units. It became clear that to combat these hazards the Army needed outside help; and a committee was set up, under the chairmanship of Dr. E. R. A. Merewether, H.M. senior medical inspector of factories, which included representatives of the three Services and of the Ministries of Health, Supply, Labour, and National Service.

PREVENTION OF DISEASE

No striking advances in prevention were made in the period under review, but research was continuously in progress.

In 1948 proguanil was substituted for mepacrine in prophylaxis against *malaria*. Proguanil causes no skin discoloration, and a shorter period of build-up is required.

A sharp increase in *diphtheria* among troops in Germany at the end of 1945 led to an inquiry into the immunisation state of recruits; and in 1946 instructions were issued for the Schick-testing, and immunisation when necessary, of all recruits. This measure is now normal practice; and in Germany, along with other more local measures, it resulted in a drop in diphtheria incidence from 3·06 per 1000 in 1946 to 0·95 in 1948.

In Germany and Austria *acute ulcerative gingivitis* also caused much anxiety. Here the only certain method of prevention was a high standard of oral hygiene and, in treatment, penicillin.

Native food-handlers in kitchens and messes were considered to be responsible for small localised outbreaks of the *enteric group* in the Middle East. It was difficult to trace the carriers owing to the intermittency of the condition. A contributory factor was the relatively low standard of accommodation and sanitation in many parts of the Middle East. Together with fly infestation, this was also responsible for much of the dysentery in the Middle East. In fact, in the years under review the incidence increased from 24·05 per 1000 in 1946 to 33·01 in 1948. The dysentery-rates for the Middle East were higher than those for the Far East. The failure to improve this situation, despite adverse factors, should be investigated further.

In 1947 there was not a single case of *cholera* in British troops or their families, though in Egypt they were living in the closest proximity to the outbreak in the Canal area; all those concerned deserve the highest credit. Reliance was placed mainly on general measures, and on the coöperation of the Forces in these measures. It was at a late stage in the outbreak, when the battle was already almost won, that popular anxiety at home led to inoculation of the troops with cholera vaccine.

Venereal disease in Germany and in the Far East caused concern in 1946. Since then there has been a steady improvement in the Far East and a dramatic drop in Germany. In the Middle East the rates were comparatively low, and in the United Kingdom low.

The introduction of chloramphenicol in 1948 completely changed the outlook for *scrub-typhus*.

Skin diseases remain, as in the past, an important cause of sickness and inefficiency. Apart from scabies, which runs parallel with venereal disease, the type of case varied with the Command. In the Far East fungus infections caused the most trouble, in the Middle East septic conditions. In 1948 a team visited the Far East to study improved methods of prevention of skin diseases. An investigation at Aldershot in the same year showed that in a random sample of 1016 newly joined National Servicemen 3·67% had tinea pedis. Communal showers and swimming-pools were thought to be more important causes than hyperhidrosis.

The average incidence of *tuberculosis* in overseas theatres was less than 1 per 1000 per annum. In the United Kingdom it was about 3 per 1000 owing to the inclusion of recruits found by mass miniature radiography to be infected on entry. Mass miniature radiography was carried out mainly by 10 mobile Army teams, but the Ministry of Labour and National Service has now agreed to this work being done at the initial medical board. Owing to shortages of staff, apparatus, and accommodation, the take-over by the Ministry is gradual, and it will be some time before the transfer is complete.

The war-time emergency vaccine laboratory at Everleigh has been transformed into an independent unit, with the title of Army Vaccine Laboratory. It has a mixed military and civilian staff divided into a bacteriological department for the preparation of immunising vaccines and diagnostic sera and suspensions, and a transfusion department for the preparation of crystalloids and the servicing of transfusion-sets. In 1948, 960 litres of T.A.B. vaccine were produced, and 198 litres of other kinds of vaccine.

PROBLEMS OF INTAKE

Psychiatric disorders accounted for 9 discharges per 1000 of the strength each year—far in excess of any other cause. Every effort was therefore made to screen thoroughly the recruits at intake centres. Personnel selection officers interview each recruit and refer to a military psychiatrist all who are so dull as to be unlikely to absorb military training or who appear to be of doubtful stability for a Service life. The rise in the percentage of intake referred from 10% in 1946 to 17% in 1948 was due rather to an increasing awareness of the value of the psychiatric screen than to deterioration in quality of the intake.

The problem of the employment of men of low intelligence remained as difficult as ever, as also the special problems of the S.G.5 group—i.e., the lowest group in terms of ability to learn—into which approximately 13% of the Army's recruit intake fell. About 5% of the Army's recruits were unable to assimilate normal training and had to be allocated to the Royal Pioneer Corps for simple labouring duties.

HOSPITAL PROBLEMS

On the surgical side in 1946–48 there was a steady decline from a first-class and fully staffed specialist service in the Royal Army Medical Corps to an overstretched service of doctors with minimum specialist cover. Furthermore, there was the general difficulty of recruiting doctors for the R.A.M.C., on account of unsatisfactory pay and conditions of service. At the same time overseas responsibilities increased greatly; for in certain commands British civilian members of the Control Commission became entitled to treatment, and the number of military families increased greatly. A high standard of surgery was, however, maintained, and a policy adopted of evacuating early from overseas long-term cases and those needing highly specialised forms of treatment.

The hospital admission-rates per annum among British troops in the four large commands over the three years were as follows (per 1000 strength):

	1946	*1947*	*1948*
U.K.	432	360	311
Germany	499	586	456
Middle East	479	390	473
Far East	685	571	551

CONCLUSION

The progressive attitude of the Army medical authorities shown in this report can reassure us all that the soldier is in excellent hands. The National Serviceman should return to civilian life physically and mentally improved, and the cumulative effect of this on the nation as a whole must be considerable. Inter-Service coöperation and liaison with the civilian medical world, which was such a profitable feature of the war years, has continued and indeed increased. Moreover, the opportunities for research in the controlled community of the Army are clearly not being lost.

In England Now

A Running Commentary by Peripatetic Correspondents

WE are daily assailed by warnings that the population is ageing, and that in 40 years a handful of wage-earners will be attempting to support a ponderous agglomeration of unproductive and senile citizens. A colleague recently pointed out to us that attention has not been adequately drawn to the increase in the rate of advance of old age, and adduces as evidence the fact that for him the millennium is here and now. Though a man of only some 38 winters, his ulcer is already well established, and his asthma and his rheumatism trouble him at night. His discs do not prolapse in a well-conducted way, but moulder away quietly, and already he has reached a stage of forgetfulness which would do credit to a stage professor. The crowning blow came the other day, when he went to his dentist for a regular check-up and was told that his teeth were being attacked by a disease of old age.

Unfortunately the potential wage-earners in his family are not yet of an age at which he can hand on the torch to them, being 6 and 2 respectively, so he is battling on despite his manifestly outworn mental and physical equipment—a man in advance of his time.

* * *

Last week I had a kind of busman's holiday attending the British Pharmaceutical Conference at Nottingham, and I found that the buses our pharmacist brethren drive are pretty complex affairs. Early in the proceedings a paper on the structural requirements for antibiotic activity in the chloramphenicol series showed me how little I know of modern pharmacological chemistry; after which the coup de grâce was administered by a discussion on polarographic determination of riboflavine. I gathered from the cognoscenti that the standard of the more esoteric papers was as high as the standard of those I could understand. In a symposium on the pharmacy of antibiotics there were some interesting remarks on what the pharmacist can teach the doctor; and, though some dissentients thought that physicians resented any such attempt, I for my part am willing to learn about all new drugs from any informed person—as indeed most of us are.

One speaker quoted Sir A. V. Hill's recent praise at the British Association for the scientific attitude of industry in this country, and claimed that the section which most deserved approbation was the pharmaceutical. There might have been a little of the "Here's tae us, wha's like us!" spirit in this, but nevertheless the conference was itself good evidence in support of the claim.

* * *

I have always prided myself on an ear for accents. I used to boast that I could spot a patient's origin and upbringing after about three sentences. But never again. After that young woman who has just left I've finished with country and class spotting for good.

"Aim a little worried about meh haht," she said. (Ah, English public school of course—Roedean, Wycombe, Cheltenham. One of those.) But the lady had not been registered before. How was that? "Well, as a metter of fect, Aim not English."

"No, no, of course not. Your name is, let me see, ah yes. Miss Pumpernickel. You will be German then?"

"Er ner, Aim not German."

"No? What are you then? You ought to be English by your accent."

"Ai expect Ai picked up meh accent from the English girls in Geneva. As a metter of fect Aim an American, and Ai wanted to awsk you if meh haht——"

* * *

The trial of suramin in cases of ocular onchocerciasis in the Gold Coast has been encouraging, but the treatment often has unpleasant side-effects—œdema of the feet and hands, severe pruritus, and sometimes loss of taste. Here is one patient's story, in his own words.

"I get four injections it begin me small. I feel from the foot it come for my hand it come for the body the skin no good at all it be tight. I get five injections it get me down I no fit get up. My tongue he bigger but no sore. I am feeling cold. If you chop something you never savvy he be good or no good. You savvy pepper. Sweet thing you never know him at all. You no fit bend your hand at all. Skin be like alligator. You feel scratch—too much, he no be small thing. All my foot make sore sore.

"That time you never inject me I never see fine. I fit shoot to here (*10 yards*). Now I fit shoot guineafowl as far as the school (*100 yards*). My eye get strong proper. Long time I never fit do this before."

This patient has at least recovered the full use of his limbs. He recently returned, on foot, from a visit forty miles away, and has been fined for beating his wife. I have no evidence on his savvying or not savvying sweet things; his wife might perhaps hold decided views.

* * *

I have to report two serious cases of hat-addiction. The first is that of a harbourmaster aged 75 who is convinced that to be bareheaded except when indoors is for him synonymous with death. Two years ago he and his son Daniel spent many anxious hours of darkness in a dinghy picking up craft of various kinds which had broken from their moorings during a heavy storm, and towing them to places of comparative safety. In the middle of one of these trying and dangerous manœuvres the harbourmaster's hat blew off. He clapped his hand in despair to his bare, bald head. "'Tis all over," he cried, "I'm gorn." Acting with prompt devotion Daniel snatched off his own hat and crammed it on to the old man's head. "No, father," he shouted, "you'm all right!" The old man is certain that his life was thereby saved.

The second case is that of a stonewaller aged 82 whose just pride it is that the walls he builds never fall down. He also works with his son, a promising kid of about 45 who should, according to his father, make a good stonewaller one day. The son states that only once has he seen his father without his hat, a battered bowler worn indoors and out, and even in bed. Five years ago the old man had to have a prostatectomy, from which he made an uneventful recovery. While he was in hospital his son visited him and walked straight past his bed. "Diddn reckernise 'im, y'see," he explained. "'E addn got 'is 'at on."

* * *

Which is the better reformer—the reasoner or the agitator? Most of us, I suppose, would say the reasoner, but when it's a matter of getting something done quickly, I fear the agitator has it. Our son, aged two and five months (2·416 yr.) obviously thinks so. My wife had dragged him into the local fish-shop, though he wanted to be at the level-crossing; and she was expecting crescendo screams of "want to see trains." But with the distractibility of children he soon noticed the flies hovering over the fish, and since he is scared of flies he informed the queue that they wouldn't hurt. Passing from the pragmatic to the more purely conceptual aspects of the fly-cloud, he said "Look at the nasty flies! What a lot of nasty flies! One, two, six, eight" (his scale of numbers has got some missing rungs). He thought this was a good word-collection, and kept on using it loudly and clearly. Most of the queue laughed, but some looked embarrassed, and others began to mutter "There *are* a lot of flies." The fishmonger himself made no comment, but he had an electric fan put in the next day. Another triumph of agitation?

* * *

The window-cleaner poked his head in. "Better now, sir?" "Much better, thank you, Tom." "What exactly is the matter, sir?" I began my prepared statement in monosyllables. "You know the bones in the back? Well, between them there are bits of . . ." "Oh, it's a disc, is it?" "So they say, Tom." "I know just what it's like: a cold wind goes right through you like a knife. It strikes the kidneys, no matter what you wrap up in. It proper doubles you up. It's quite the fashion these days, though I never heard tell of it before. It could be these artificial fertilisers they put everywhere, don't you think so? Myself, I think it's rheumatics. Well, so long sir, take it easy." He disappeared down his ladder.

Letters to the Editor

SELECTION OF MEDICAL STUDENTS

SIR,—In the interesting discussions on this subject in your issue of Aug. 30 little or no attention was given to the *size* of the problem.

About 2700 medical students are accepted annually; no-one seems to know what is the total number of applicants. At University College it seems that 600 students apply for 60 places; at less well favoured schools the ratio of applicants to places is apparently 7, 6, or 5 to 1. But it is well known that students generally apply to many schools, sometimes to all, in the hope of being admitted somewhere. The total number of university undergraduate students in all faculties is about 84,000—or, say, about 25,000 in each year of study. Is it to be supposed that all or even a substantial proportion of the students in the faculties other than medicine wanted to do medicine but failed to find a place? One occasionally meets a student who failed to be accepted anywhere, but there is no evidence that such cases are numerous; there is, for instance, no association of indignant rejected applicants. The matter could easily be settled if all candidates were required to fill in their application forms in duplicate, and one of the copies was sent to a central registry which collated the information. I gratuitously suggest that such a registry might be set up by the General Medical Council, the Royal Colleges, the ever helpful Nuffield Trust, or one of the universities. I hazard a guess that such an inquiry would show that the majority, perhaps the great majority, of those wanting to do medicine find places, although not necessarily in the school of their first choice.

I think we are too ambitious in our attempts at student selection: we aim at choosing the best; we should be satisfied to exclude the worst. We, of course, all know the ideal student: tall, handsome, of great personal integrity, beautifully mannered, cultured, highly intelligent, a tireless worker, original, good with his hands, skilful in exposition, a good mixer, athletic, devoting his spare time to extramural activities, with a good family background, and so on and so forth. But, of course, such students do not exist. The qualities required for success in the many occupations which a doctor can take up are so varied that I imagine that no group of selection tests, however elaborate, can be reliable. How is one to select, say, the future editor of THE LANCET, the medical officer of a Polar expedition, or an able academic research-worker? What, however, we can and must do is to exclude the student who is unlikely to display a certain minimum standard of intellect and industry; I suggest that this minimum might be the ability to get a pass or a near-pass at the 2nd M.B. at the first attempt and to get through without undue effort at the second attempt (should that be necessary). As some of your correspondents have pointed out, a candidate's school record and an honest report from the school authorities are a fair guide; the standard of performance at the 1st M.B. or the higher school certificate is even more helpful. But one should always allow for a margin of error of, say, 10–15%; and some deans, in deciding the number to be admitted, assume that a small proportion of their students will fall by the wayside for one reason or another.

The statistical inquiry that I have suggested will probably show that more students of the minimum standard set out above apply than there are places for. I doubt whether it is worth trying to sift them too thoroughly. Any method used will reject candidates who are as good as those who are selected. By allowing deans or selection committees scope for their individual whims and fancies we shall probably get students with the wide range of valuable supplementary qualities that the community needs.

Department of Physiology,
Middlesex Hospital Medical School,
London, W.1. SAMSON WRIGHT.

HÆMOPOIESIS IN THE FŒTUS

SIR,—When I first became interested in hæmatology some thirty years ago, it was customary to describe megaloblastic blood formation as seen in cases of pernicious anæmia as a reversion to an embryonic or fœtal type of hæmopoiesis. Presumably this conception was largely based on the original description by Ehrlich, who gave the name of "megaloblast" to certain primitive nucleated red cells in the embryo. The modern view is that megaloblastic blood formation results from a deficiency of certain hæmopoietic factors (vitamin B_{12}, folic acid, &c.). Since there is no reason why the fœtus should be deficient in these factors, it seemed to me difficult to understand why fœtal hæmopoiesis should be megaloblastic.

Accordingly, I decided to examine films made from the bone-marrow and from the juice expressed from the cut surface of the liver of embryos of different ages. The films were stained with Leishman's stain. Dr. Agnes Macgregor, pathologist, was able to provide me with bone-marrow films and liver-juice films from one fœtus of 16 weeks, one of 20 weeks, two of 22 weeks, two of 26 weeks, and one of 34 weeks. In every instance blood formation was normoblastic in type, and most of the nucleated red cells were late normoblasts with late pyknotic nuclei.

Department of Medicine,
University of Edinburgh. L. S. P. DAVIDSON.

A.C.T.H. AND ASCORBIC ACID

SIR,—Since the preliminary communication by Lewin and Wassén [1] there have been many reports concerning the action of ascorbic acid on rheumatoid and formalin arthritis. On the basis of our observations on the potentiation of the thymolytic effect of A.C.T.H. by ascorbic acid (unpublished data), we performed the following experiment.

In normal male albino rats, weighing 130–150 g., formalin arthritis was produced by injecting 0·1 ml. of 2·5% solution of formalin beneath the plantar aponeurosis of the right hind-leg. The inflammation of the joints was assessed by measuring daily the volume of the extremity by Bacchus's method.[2]

In the first part of the experiment 25 animals with formalin arthritis were divided into five groups and treated daily with A.C.T.H. (Armour) subcutaneously and ascorbic acid (A.A.) intraperitoneally. The data are briefly presented in table I.

TABLE I—EFFECT OF A.C.T.H. AND ASCORBIC ACID IN ARTHRITIC RATS

Group	Daily treatment	Swelling of the leg (c.cm.)*
1	1 mg. A.C.T.H. in 0·5 ml. 1 ml. 0·9% NaCl	0·314 ±0·024
2	0·1 mg. A.C.T.H. in 0·5 ml. 1 ml. 0·9% NaCl	0·356 ±0·039
3	50 mg. A.A. in 1 ml.	0·343 ±0·016
4	1 mg. A.C.T.H. in 0·5 ml. 50 mg. A.A. in 1 ml.	0·125 ±0·014
5	0·1 mg. A.C.T.H. in 0·5 ml. 50 mg. A.A. in 1 ml.	0·209 ±0·026

* Mean value of all measurements over a period of 6 days and standard error of the mean.

There was a significant difference between the animals treated with 1 mg. A.C.T.H. daily, and the group that received the same dose of A.C.T.H. combined with ascorbic acid ($p<0·001$). In the same way the addition of ascorbic acid

1. Lewin, E., Wassén, E. *Lancet*, 1949, ii, 993.
2. Bacchus, H. *Endocrinology*, 1951, **49**, 789.

TABLE II—EFFECT OF CORTISONE AND ASCORBIC ACID IN ADRENALECTOMISED ARTHRITIC RATS

Group	Daily treatment	Swelling of the leg (c.cm.)
1	1 mg. cortisone in 0·5 ml. 50 mg. A.A. in 1 ml.	0·440 ±0·013
2	1 mg. cortisone in 0·5 ml. 1 ml 0·9 % NaCl	0·420 ±0·013

increased the effect of a dose of 0·1 mg. A.C.T.H. ($p<0·01$). Finally, there was a significant difference in the presence of ascorbic acid between 1 mg. and 0·1 mg. A.C.T.H. ($p<0·01$), whereas without ascorbic acid there was no statistically significant difference between these doses ($p>0·05$). Ascorbic acid alone did not modify the formalin arthritis more than A.C.T.H. alone.

In the second part of the experiment we tried to exclude a peripheral synergism of cortisone (Merck) and ascorbic acid. 10 adrenalectomised animals with formalin arthritis were given cortisone subcutaneously and ascorbic acid intraperitoneally. The results are given in table II.

This table shows that the activity of cortisone applied in these doses cannot be potentiated by ascorbic acid ($p<0·05$). This experiment indicates that there is neither a peripheral synergism of corticoids and ascorbic acid, nor a peripheral sensitisation of the tissues by ascorbic acid to the action of corticoids.

These experiments accord with the well-known, but not generally accepted, assumption that ascorbic acid acts at the level of the adrenal gland on the synthesis of corticoids.[3] There is, however, still another possibility—that A.C.T.H. is inactivated at a slower rate in the presence of large quantities of ascorbic acid.

These experiments were carried out at the Institute for Industrial Hygiene, Yugoslav Academy of Science, Zagreb.

Lj. Božović
Medical Faculty, S. Milković.
University of Zagreb, Yugoslavia.

OBSERVATION ON WHOOPING-COUGH

Sir,—I should like to record a personal clinical observation.

At the end of August, 1951, I had the misfortune to develop whooping-cough, having caught it from my 3-year-old daughter, who in turn had caught it from her 5-year-old cousin. During the 2nd week of my attack, I developed an area of hyperæsthesia in the posterior part of each external auditory meatus, and any stimulus (such as the introduction of an aural speculum) to this area induced a typical attack of paroxysmal coughing. After about 6 weeks this phenomenon ceased, and stimulation of this area did not produce any cough at all.

I suggest that this observation adds, although slightly, to the evidence in favour of the paroxysmal stage of whooping-cough being due to a toxin produced by *Hæmophilus pertussis*, rather than to the accumulation of secretions following damage to the cilia [4] or to enlargement of the tracheobronchial glands. Damage to the cilia and enlarged tracheobronchial glands occur in many other conditions, but the typical paroxysmal cough terminating in vomiting is rare except in whooping-cough.

That *H. pertussis* produces an endotoxin has been known since the original papers of Bordet and Gengou (1906). More recently Evans and Maitland [5] have studied the characteristics of a thermolabile toxin, and Flosdorf and Kimball [6] have described a thermostable toxin. Thompson [7] prepared an endotoxin which he used therapeutically. He noticed that a few hours after subcutaneous injection there was exacerbation of coughing paroxysms. Many physicians believe that convulsions and encephalitis may sometimes be due to the toxin [8]; and Laurent [9] and Dolgopol [10] hold that on rare occasions a secondary encephalitis reaction may be observed in addition to the circulatory lesions. There is, therefore, evidence for the production of a neurotoxin, and some workers [8] consider that this toxin sensitises nerve-endings in the respiratory mucosa to external stimuli. In consequence of the observation recorded above, I would suggest that the toxin acts on the vagus nerve, after the fashion of tetanus toxin, the (?) toxin of eclampsia, and strychnine, all of which sensitise the nervous system so that it reacts violently to trivial stimuli.

Further circumstantial evidence to the hypothesis that the catarrhal stage of whooping-cough is due to local infection with *H. pertussis* whilst the paroxysmal stage is due to a neurotoxin is found in the reports on treatment of whooping-cough with the modern antibiotics. Most workers agree that the best results are obtained if chloramphenicol is given within the first 2 weeks of the disease, the treatment having little effect once the paroxysmal stage is really established.[11] This observation is analogous to the neuritic complications of diphtheria, in that by the time the paralyses develop in diphtheria the local bacterial infection has usually ceased to be significant. The action of the pertussis neurotoxin, however, would appear to be excitatory rather than depressant.

London, W.5. M. D. Warren.

BOXING CONTESTS

Sir,—I would be interested to know if Dr. Blonstein could justify his statement last week that boxing fosters a high physical and moral standard in the nation's youth.

Physically the muscular development produced by training will raise the performer's ability for muscular work, but much of this is temporarily or even permanently offset by injuries. I do not know of any evidence that muscular development protects an individual against disease. During my Service life in the R.A.F. I looked after a physical-training school, where the sickness-rate was as high as among other airmen and the accident-rate much higher.

As regards moral betterment I feel that Dr. Blonstein has a much weaker case. The training of individuals to dominate each other by physical force is surely a poor training in social adaptation and peace.

The educational effect of watching such contests is about as high as that of reading the baser comics.

Middlewood Hospital, Sheffield. G. I. Tewfik.

HICCUP DURING ANÆSTHESIA

Sir,—Most of the letters on this subject have referred to hiccup during upper abdominal operations. I should like to describe a case where it occurred during an appendicectomy.

A healthy male European, aged 32 and weighing 12 st. 8 lb., was admitted with lower abdominal pain and vomiting of $2^1/_2$ hours' duration.

At operation he was given sodium thiopentone (1·5 g.) and 'Flaxedil' (80 mg. followed by 60 mg.). The operation lasted 40 min. He started to hiccup when the appendix was pulled upon, and he stopped when the appendix was severed.

The second dose of flaxedil was given during the period of hiccup; nitrous oxide was given to dilute the oxygen, but had no effect.

I can offer no explanation of this case, but I think it is worth recording.

Jokai Central Hospital, Assam. D. A. H. McNaught.

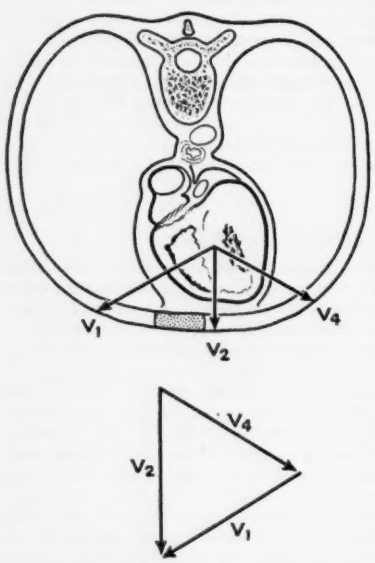
3. Lowenstein, B. E., Zwemer, R. L. *Ibid*, 1946, **39**, 63.
4. Pullen, R. L. Communicable Diseases. London, 1950.
5. Evans, D. G., Maitland, H. B. *J. Path. Bact.* 1937, **45**, 715.
6. Flosdorf, E. W., Kimball, A. C. *J. Immunol.* 1940, **39**, 475.
7. Thompson, A. R. *Lancet*, 1937, ii, 733.
8. Harries, E. H. R., Mitman, M. Clinical Practice in Infectious Diseases. Edinburgh, 1951.
9. Laurent, L. J. M. *In* Modern Practice in Infectious Fevers. Ed. H. S. Banks. London, 1951.
10. Dolgopol, V. B. *Arch. Neurol. Psychiat.* 1941, **46**, 477.
11. Swift, P. N. *Lancet*, 1948, i, 133. Gray, J. D. *Ibid*, 1950, ii, 800. Lassen, H. C. A., Grandjean, L. C. *Ibid*, 1951, i, 763. Bogdan, A. *Ibid*, ii, 1204.

LEADS IN ELECTROCARDIOGRAPHY

SIR,—We would like to make some comments on your leading article on this subject (May 31).

The different leads used in electrocardiography can be set out usefully and clearly by a geometrical method. The classical Einthoven's triangle is an example of how to represent the three standard leads. But any lead can be defined by a segment of a straight line orientated in space [1]: we call this line the axis of the lead. The axis of a unipolar lead lies on the straight line connecting the centre of the heart with the exploring electrode. The axis of a bipolar lead does not always lie on the line connecting the two electrodes, but can be found in a simple geometrical way.

What we record in any lead is the projection of the electrical vectors upon the axis of the lead. The axes of the standard leads are situated in the frontal plane, and therefore they record the electrical activity of the heart, projected on the frontal plane. The axes of the precordial leads are situated in the horizontal plane, and therefore one would expect them to record the same phenomenon as the standard leads, projected on the horizontal plane. But a different conception has been widely accepted: these leads have been thought to record almost exclusively the activity of the myocardium immediately beneath the exploring electrode. This conception may seem justified by the fact that the precordial leads are unipolar and the exploring electrode is near the heart. In fact such a fundamental distinction between bipolar and unipolar leads is not justified. What defines any lead, either unipolar or bipolar, is its axis.



It has been shown experimentally, for instance, that a unipolar and a bipolar lead record the same tracing when their axes are parallel.[2] Actually the similarity usually seen between I (bipolar and limb lead) and V6 (unipolar and precordial lead) is due to the similar orientation of their axes.

We submit that the proximity of the exploring electrode to the heart is quite relative, and does not allow any great "selectivity" in differentiating the various parts of the heart.

It has been shown [3] that, as a rule, the precordial leads record the activity of the heart in toto, and not of a single part of it. Moreover it is well known from physics that to put an electrode very near to an electrical source of energy is not always the best method of recording a higher potential; if the electrode is, for instance, on the perpendicular to the vector representing the electrical source—i.e., equidistant from its negative and positive sides—there will be no potential recorded, however near to the electrical source the electrode may be. Other objections have been raised to the so-called "local effect" theory.[4–6]

We think it is unjustifiable to consider the precordial leads to be so different from the limb leads as to need the interpretation that has been given them in English-speaking countries. Both the standard and the precordial leads obey the law of the projection of the electrical vectors upon the axes of the leads, and they record the same phenomenon; only the plane of the projection is different.

In other words, the same relationship exists between standard and precordial leads as, for instance, between anteroposterior and lateral or oblique views of the thorax in radiology. The analogy between standard and precordial leads is such that it is possible to find a system of three precordial leads which form, with their axes, a horizontal equilateral triangle, similar to the frontal one of Einthoven.[7]

The accompanying figure shows the axes of these three leads, and the equilateral triangle formed by them.

With the "local effect" theory one must always accept the possibility that a part of the heart may have escaped exploration, however numerous the precordial leads; but we feel that the examination can be satisfactorily carried out with these three leads alone. We think therefore that the precordial leads should be interpreted in the same general way as the standard leads.

ALDO SELVINI
AUGUSTO PILOTTI
FRANCO LANZA.

Medical Clinic of the University, Milan.

1. Selvini, A., Pilotti, A., Lanza, F. *Cardiologia*, 1950, **16**, 92.
2. Selvini, A. *Folia Cardiol., Milano*, 1943, **4**, 213.
3. Duchosal, P. W., Sulzer, R. La vectocardiographie. Basle, 1949.
4. Spang, K. *Z. KreislForsch.* 1949, **38**, 405.
5. Holzmann, M. *Ibid.* 1951, **40**, 577.
6. Schaefer, H. Das Elektrokardiogramm: Theorie und Klinik. Berlin, 1951.
7. Selvini, A. Communication to the 13th Congress of Italian Cardiology: Naples, 1951 (in the press).

COMPLICATIONS OF CONTROLLED HYPERTENSION

SIR,—In your leading article of July 5 you refer to a report of mine [8] on the effect of intravenous hexamethonium bromide on kidney function.

I should like to correct the impression conveyed by your article that the dose used each time was 100 mg. In fact, this very large dose was used in only one patient, who had already become habituated to the drug. In the remainder the dose varied from 15 to 50 mg.

E. GARTH MCQUEEN.

Department of Medicine, University of Queensland, Brisbane, Australia.

8. McQueen, E. G. *Med. J. Aust.* 1952, i, 769.

NICOTINIC ACID AND BURNING FEET

SIR,—A 31-year-old man with lupus vulgaris of the face was treated with isonicotinic acid hydrazide 150 mg. daily by mouth. After one week's treatment he developed a severe burning sensation of the soles of the feet—"as if there was a fire under my feet." This sensation continued for 2 days after the tablets were discontinued. He then, of his own accord, took a reduced dose of 50 mg. daily for 3 weeks without ill effect. The patient has always had hyperhidrosis of the feet, and on one occasion he developed a mild burning sensation in the feet while taking medicine of unknown nature.

The symptoms in this case recall the "burning feet" syndrome described in India and in Japanese prisoner-of-war camps. This syndrome is characterised by severe burning or freezing sensations in the feet, accentuation of the reflexes, and hyperhidrosis of the feet. While accentuation of the reflexes is a well-recognised effect of isonicotinic acid hydrazide, burning feet has not been reported before, as far as I am aware, as a toxic effect of the drug. The hyperhidrosis was present already in this case and so cannot be ascribed to the action of the drug. Gopalan [9] has ascribed the "burning feet" syndrome to deficiency of pantothenic acid, but the findings in the case described here suggest that nicotinic-acid deficiency may play a part in the ætiology of this condition, since isonicotinic acid hydrazide may conceivably block the action of nicotinic acid by competitive inhibition.

London, S.W.1. J. S. PEGUM.

9. Gopalan, C. *Ind. med. Gaz.* 1946, **81**, 22.

CHLORAMPHENICOL IN ERYSIPELOID OF ROSENBACH

SIR,—I have found that chloramphenicol inhibits in vitro the growth of *Erysipelothrix rhusiopathiæ*, and I recently gave the drug to 4 patients with erysipeloid of Rosenbach, 2 of whom had not responded to treatment with penicillin.

Doses of 2 g. per day produced rapid resolution in 3 cases; in fact, after the first day of treatment, pain, œdema, and erythema quickly subsided, and after the third day only pigmentation and desquamation remained.

The 4th case was more resistant, and vivid-red erythematous areas persisted at the circumference of the lesion. But healing was complete after five days' treatment. Supplementary local treatment with 2% chloramphenicol in a base of 'Carbowax' produced no local or general intolerance.

This is insufficient evidence for a definite conclusion, but it justifies further study of the drug in erysipeloid.

Dermatology Clinic,
University of Bologna,
Italy. PAOLO MORONI.

MALARIA

SIR,—I feel humble and appreciative in respect of your review (Aug. 30) of my book on *Malaria*. One point, however, disturbs me. I want to make it clear that I have the highest respect for, and I accept, the work of Shortt and Garnham and their colleagues on the pre- and exo-erythrocytic stages of malaria plasmodia. My term "in the shadows," referring to these early forms of the parasite, seemed fair when I wrote it because the earliest development following the sporozoite had not been described by any observer. Even today, although further progress has been made, there remain points that are not clear. It was not my intention to reflect on the fundamental studies mentioned, to which in fact I gave full credit in the short historical chapter of the book.

Division of Medicine and Public Health,
Rockefeller Foundation,
European Office, Paris. PAUL F. RUSSELL.

SORE THROAT AND RHEUMATIC FEVER

SIR,—In his letter (Aug. 16) Dr. Collis asserts that "Schlesinger's contribution was his observation of the silent period between the initial throat infection and the subsequent rheumatic-fever attack, or relapse, and the effect on the subsequent attack of salicylate if given during the silent period."

Schlesinger, as far as I know, has never claimed that he first observed the silent period, although he was an ardent advocate of salicylate therapy, as he made clear in his Milroy lectures of 1938.[1] I suggest that the chief credit for observing the silent period goes to C. Haig-Brown, who in *Tonsillitis in Adolescents* (1886) wrote:

"An attack of acute rheumatism is very frequently preceded by one of acute tonsillitis, it may be by as long a time as five or six weeks, but more usually ten days or a fortnight; while, as has been already stated, the two may be coincident in time. In fact, it is rare to meet with a case of rheumatic fever which has not been recently preceded by a sore throat; and though I am not prepared to say that tonsillitis is the fore-runner or the companion of every case of rheumatic fever, the last eleven cases of the latter which I have had to treat have, within six weeks of the onset of the joint-pains and fever, been under my hands with sore throats."

This was probably not the original description, for Haig-Brown modestly says:

"As has been observed by others than myself, it is very frequently found that the subject of articular rheumatism has had a 'sore throat' perhaps a month, but more commonly ten days or so, before he felt pain in his joints, or that simultaneously with the joint-affection, there is tonsillitis."

Rugby. R. E. SMITH.

1. Schlesinger, B. *Lancet*, 1938, i, 593, 649.

MEPACRINE AND RHEUMATOID ARTHRITIS

SIR,—We have read with interest the preliminary communication by Dr. Freedman and Dr. Bach (Aug. 16). Since Page's[1] report appeared, we have used mepacrine on a limited scale in selected cases.

A young woman with acute lupus erythematosus was dangerously ill when treatment with A.C.T.H. was started. She improved rapidly, but on account of side-effects of A.C.T.H. we tried mepacrine with apparently good results. The withdrawal of mepacrine was followed by deterioration.

We have given mepacrine to 11 patients with rheumatoid arthritis. The longest period of observation is five months and the shortest six weeks. All of the patients declared that their pain gradually eased, and in 5 there is already definite objective improvement. Treatment with mepacrine is not followed by eosinopenia or increased excretion of 17-ketosteroids; nor is the erythrocyte-sedimentation rate or temperature influenced in our experience.

During the last two years, 2 patients with bronchial asthma have been admitted to our hospital repeatedly on account of status asthmaticus. Several times we have had to use A.C.T.H. for short periods. Six months ago we started giving these 2 patients mepacrine. Follow-up examinations have shown that both are entirely free of symptoms and signs of bronchial asthma.

We agree with Freedman and Bach regarding dosage and length of treatment. The variable course of rheumatoid arthritis and bronchial asthma makes it very difficult to differentiate between a spontaneous remission and an effect of administering mepacrine. We hope that extended trials of mepacrine will soon solve this problem.

Medical Department,
Rogaland County Hospital,
Stavanger, Norway. ARNFINN ENGESET.

AVERSION TO ALCOHOL

SIR,—The chance observation by Dr. Walker and Dr. Boyd (Sept. 6) that a heavy beer drinker exposed to tetraethyl lead (T.E.L.) abruptly stopped drinking (and also developed a voracious appetite) a few weeks before being admitted to hospital for T.E.L. poisoning, is of great interest to those engaged in the study and prevention of alcoholism. The same voracious appetite and distaste for alcohol was observed in 1938 in a number of workmen exposed in a clay pit to hydrogen sulphide.[2] The advent of 'Antabuse' (not 'Antabus' as recently adopted by THE LANCET) has stimulated interest in substances—of which there are quite a number[3]—causing aversion to or distaste for alcohol, which are not the same things.

In the case of antabuse it is an aversion, for one avoids contact with alcohol because of the unpleasant symptoms which then supervene. A similar aversion appears to exist in the initial stages of Hodgkin's disease, where pain, cough, and itching become intensified on taking even small amounts of alcohol.[4] On the other hand, hydrogen sulphide appears to produce a distaste, no other symptoms except the voracious appetite being reported.

Chance observations such as these may help us eventually to find a means of readjusting physiological imbalance as the cause of alcoholism. This society is anxious to collect further observations of the kind, especially on substances producing distaste or disinclination for alcohol.

H. PULLAR-STRECKER
Hon. Secretary,
Society for the Study of Addiction.
Wyke House, Isleworth,
Middlesex.

1. Page, F. *Lancet*, 1951, ii, 755.
2. *Brit. J. Addict.* 1949, **46**, 47.
3. See *Ibid*, 1951, **48**, 72.
4. Verbeeten, B. *Med. Tijdschr. Geneesk.* 1952, **96**, 13.

ANTITHYROID ACTION OF P.A.S.

SIR,—Clausen and Kjerulf-Jensen [1] have described three cases of thyroid enlargement with myxœdema during *p*-aminosalicylic acid (P.A.S.) therapy, and Komrower [2] has reported another. I should like to add a further case.

An unmarried woman, aged 23, was admitted to hospital on July 3, 1951, with pulmonary tuberculosis of two years' duration, clinically affecting the right lower lobe. A chest radiograph showed, in addition to the disease at the right base, some apparently new lesions at the left base. In view of this, chemotherapy was decided upon. Thiosemicarbazone ('Ethizone') (starting dose 50 mg., then 150 mg. daily) and sodium P.A.S. (3 g. four-hourly) were given.

On Sept. 17 (eleven weeks later) she complained of a swelling in the neck, and a soft diffuse, non-pulsatile, slightly tender swelling of the thyroid gland was felt. The pulse-rate was normal and the blood-pressure was 100/70 mm. Hg. There was no exophthalmos or sweating. Both drugs were stopped immediately; a total of 1170 g. of P.A.S. and 7·75 g. of ethizone had been given. She was watched for further signs of disturbed thyroid function, but none developed.

Five weeks later (Oct. 23) the swelling had subsided. The chest radiograph was unchanged. Further progress was uneventful; the left basal signs subsided, leaving the right side unchanged.

On June 18, 1952 (about eleven months later), the thyroid gland was just palpable. Her weight had remained steady at 7st. 7½ lb.

The patient has an immature and hysterical personality. She has had an unhappy home life with life-long episodes indicative of instability and insecurity. She is prone to temper-tantrums and on Jan. 1, 1952, had a prolonged episode of this sort. A psychiatrist advised certification if she proved difficult to manage, but she has since been quiet and coöperative.

Investigations.—Sept. 22, 1951: Sputum contained scanty atypical acid-fast bacilli; barium swallow normal; laryngoscopy, no gross tracheal compression; erythrocyte-sedimentation rate 4 mm. in first hr. (Westergren) at room-temperature; white blood-cell count 4400 per c.mm. (polymorphs 61%, lymphocytes 20%, monocytes 4%, eosinophils 14·5%, basophils 1%); blood-cholesterol 270 mg. per 100 ml.; basal metabolic-rate −22 (a further test was refused); weight 7 st. 9 lb.

Dec. 18: Hb 87%; blood-cholesterol 100 mg. per 100 ml.; weight 7 st. 13 lb.

It was natural to speculate whether either of the two drugs had caused the thyroid depression.

Bergqvist and de Mare [3] described a patient who died of hypothyroid goitre and cerebral œdema after treatment with 'Conteben,' and another who had definite hypothyroid symptoms after prolonged treatment with P.A.S., dihydrostreptomycin, and conteben. Domagk [4] however had never heard of an instance during conteben therapy. Mertens and Bung [5] did not mention thyroid enlargement in a review of conteben toxicity, neither did the report of the pilot trial of the British Tuberculosis Association [6] or Nagley's review of thiosemicarbazones.[7] A full account of anti-thyroid drugs by Suter [8] also made no reference to it. For these reasons, ethizone was discounted.

That P.A.S. could be responsible is borne out by Komrower's case [2] and the 3 Norwegian cases.[1] In the case described here, apart from the thyroid swelling, lowered B.M.R., and high normal blood-cholesterol, there were no overt signs of hypothyroidism, unlike the other reported cases. Unfortunately the patient refused a further B.M.R. test, and return to normal had to be judged clinically. The high eosinophil-count is interesting and may be evidence of drug allergy.

Kjerulf-Jensen and Wolffbrandt [9] have shown that rats fed with P.A.S. and *m*-aminophenol developed moderate cellular hyperplasia of the thyroid gland. Using radioactive iodine, Hanngren [10] found that uptake of iodine in the thyroid gland during P.A.S. therapy was inhibited in 3 patients. He thought that enlargement of the thyroid was compensatory, and caused by increased formation of pituitary thyrotropic hormone. He considered that when P.A.S. is given therapeutically a certain blood concentration will inhibit thyroxine synthesis just as thiouracil does. Doses in excess of the patient's thyroid sensitivity may cause myxœdema.

As in the other cases, the therapeutic effect of P.A.S., if any, did not appear to be antagonised by its antithyroid effect, which may even be beneficial in itself. The metabolic-rate is usually normal in active tuberculosis,[11] but whether a decreased rate is an advantage is debatable.

Nash [12] however gave thiouracil to 3 patients in 1947, with unexpected spread of the tuberculous lesions as a result. I remember a girl, aged 16, with thyrotoxicosis and pulmonary tuberculosis who was treated with thiouracil in 1945, and the tuberculosis became worse. It is interesting to note that Madigan et al.[13] suggested that the B.M.R. might rise during P.A.S. therapy, though whether a rise precedes a fall is speculative in the absence of serial tests.

The effect of myxœdema on tuberculosis is of interest. Pagel [14] merely stated that affections of the thyroid are reputed to be associated rarely with tuberculosis—i.e., they are antagonistic to its development. Other authorities [15–17] are more pessimistic, and say that untreated cases of myxœdema may die of intercurrent infections such as tuberculosis—i.e., their resistance to the disease must be lowered.

In the case reported here gross swelling of the thyroid subsided within five weeks of stopping the drugs, though it was still palpable after one year. Obviously the longer administration is continued after the thyroid swelling has appeared, the greater is the risk of myxœdematous change. Komrower's case developed after nine months' treatment. The short period of three months in this case perhaps explains the minimal thyroid changes. Whether irreversible damage can occur is speculative.

Alternatively the thyroid swelling could be ascribed to an unstable endocrine system associated with mental instability, but the lowered B.M.R. is against this. Nash [12] wondered whether the antithyroid effect of P.A.S. could exist *without clinically obvious hypothyroidism*. This case suggests that it can.

I should like to thank Dr. J. Spencer and Mr. J. Mallard, A.I.M.L.T., for the metabolic investigations, Mr. L. Whittaker, A.I.M.L.T., for the other investigations, and Dr. G. L. Brown for his help.

Ilford Isolation Hospital,
Chadwell Heath, Essex. I. M. LIBRACH.

AMŒBIC ABSCESS OF BONE

SIR,—Amœbic abscesses have now been described in many tissues of the body. In this part of West Africa, where amœbiasis is heavily endemic, it has to be considered in the differential diagnosis of many clinical conditions.

I have recently had under my care an African man of the Mende tribe who complained of a hard painful lump in the middle of his thigh. Two years ago he was treated at this hospital for amœbic dysentery with a course of 6 injections of gr. 1 of emetine. There was no recurrence of dysenteric or other symptoms until the onset of fever, malaise, and pain in the left thigh one month before I saw him.

The patient was emaciated and looked ill; on the middle third of the left femur there was a tender mass about 8 cm. long; it was fixed to the bone, and though firm it was not bony hard; there was no detectable fluctuation, although the mass was clearly palpable through the wasted muscles. X-ray

1. Clausen, A. K. H., Kjerulf-Jensen, K. *Nord. Med.* 1951, **45**, 475.
2. Komrower, G. M. *Brit. med. J.* 1951, ii, 1193.
3. Bergqvist, N., de Mare, O. *Nord. Med.* 1951, **45**, 474.
4. Domagk, G. *Irish J. med. Sci.* 1951, p. 474.
5. Mertens, A., Bung, R. *Amer. Rev. Tuberc.* 1950, **61**, 62.
6. British Tuberculosis Association. *Tubercle*, 1951, p. 217.
7. Nagley, M. M. *Practitioner*, 1952, **168**, 523.
8. Suter, C. M. *In* Medicinal Chemistry. New York and London, 1951; vol. i, p. 105.
9. Kjerulf-Jensen, K., Wolffbrandt, G. *Acta. Pharmacol. scand.* 1951, **7**, 376.
10. Hanngren, A. *Lancet*, 1952, ii, 117.
11. Kayne, G. G. *In* Pulmonary Tuberculosis by G. G. Kayne, W. Pagel, and L. O'Shaughnessy. London, 1939; p. 306.
12. Nash, F. A. *Lancet*, Aug. 2, 1952, p. 245.
13. Madigan, D. G., Griffiths, L. L., Lynch, M. J. G., Bruce, R. A., Kay, S., Brownlee, G. *Ibid*, 1950, i, 239.
14. Pagel, W. *In* Pulmonary Tuberculosis. London, 1939.
15. Fishberg, M. Pulmonary Tuberculosis. Philadelphia, 1932.
16. Tidy, H. L. Synopsis of Medicine. London, 1939; p. 874.
17. Rich, A. R. Pathogenesis of Tuberculosis. Springfield, Illinois, 1946.

examination was not available; the fæces contained mature cysts of *Entamœba histolytica*.

After several days' rest in bed with hot fomentations to the thigh, the mass began to soften and was explored with a needle. 3 ml. of a thick, dirty white pus was aspirated, and this contained many active *E. histolytica*; no other organisms were found in stained smears.

Six daily injections of gr. 1 of emetine were given, after which the mass had subsided, leaving no apparent thickening of the bone nor any tenderness. The patient was seen one month later when he was in much better health and gaining weight. The thigh appeared normal and had given him no trouble.

This is a case of metastatic amœbic abscess occurring, presumably, deep to the periosteum of the femur. There was no history of trauma to explain the site of the lesion; and although it had been there at least one month there can have been little, if any, new bone formation around it. The rapid and apparently complete cure also implies the absence of bone destruction on any large scale. In view of the extensive destruction of other tissues exposed to the cytolytic powers of this amœba, it would be interesting to know its action on bone in the absence of secondary infection. This case again raises the question of the mode of spread of the organism within the body. It also indicates that it is not, perhaps, so effective in its attack on bone as on, say, the liver.

Methodist Hospital, Segbwema, Sierra Leone. J. R. ROSE.

PROLONGED APNŒA

SIR,—There have been several reports of prolonged apnœa following "balanced" anæsthesia with thiopentone together with succinylcholine.

After carefully reading these reports I cannot see that a clear case against succinylcholine has been established in any one case. In my experience of administering thiopentone with a relaxant there have been a few instances of prolonged apnœa; and in each such case the mode of recovery, and the signs accompanying it, have clearly pointed to thiopentone as the cause.

In my experience the response to, and the recovery-time from, a given dose of a relaxant drug varies very little with either the age or the physical condition of the patient. Indeed I have repeatedly been surprised at the tolerance to these drugs of aged and very sick patients, including some aged over 70 and desperately ill with intestinal obstruction. It has been my impression that these patients require relatively more relaxant than the fit younger patients. My experience with thiopentone is quite the reverse of this; not only is there a progressive decrease in the tolerance of patients for this drug with advancing years and deteriorated physical condition (either from shock or toxæmia), but there is also a disconcerting variation in the tolerance of individual patients in the same age-groups irrespective of their physical condition. For these reasons, if my observations are correct, prolonged apnœa after administration of thiopentone together with a relaxant is many times more likely to have been caused by the thiopentone than by the relaxant.

In no case in my experience, nor in the cases reported, has consciousness returned before the restoration of breathing—a state for which I have many times been profoundly grateful. We know from experimental evidence that even massive doses of relaxant drugs have no effect on consciousness, provided that artificial respiration is adequate; and the same is true of suspended respiration due to the action of local analgesics or of the virus of anterior poliomyelitis on the motor nerves. Thus when unconsciousness accompanies and outlasts suspended respiration after the administration of a relaxant and a hypnotic, which is also a powerful respiratory depressant, the cause must surely be the hypnotic.

Once active respiration is suspended and controlled respiration has been instituted, other factors tend to prolong apnœa. Manually controlled respiration by compression of a reservoir bag usually tends to maintain a tidal volume much in excess of the normal. If this controlled respiration is carried out with an absorbing canister in circuit, as it should be, the overventilation causes such hyperoxygenation, carbon dioxide depletion, and exhaustion of the Hering-Breuer reflex that it may prolong apnœa indefinitely. Many a seemingly interminable apnœa can be ended by discontinuing controlled respiration for a few minutes. I think that apnœa produced by overventilation may have played a not inconsiderable part in prolonging apnœa initiated by either the relaxant or the thiopentone. It should be remembered that it is more easy to produce apnœa by overventilation in the presence of central respiratory depression than to abolish the peripheral neuromuscular mechanism by the same means.

I have observed two signs which determine whether the apnœa is primarily due to central or to peripheral respiratory depression.

The first sign of restoration of the neuromuscular mechanism following full curarisation is rhythmical tone in the muscles of respiration. This muscle-tone appears some time before active muscular contractions take place; its presence is indicated by the feeling of resistance when the reservoir bag is compressed out of phase with the returning respiratory rhythm. This resistance to inflation may be mistaken for evidence of the return of abdominal-muscle tone and lead to the administration of a further dose of relaxant; or, if the bag compressions are completely out of phase, the resistance to inflation, in the presence of a relaxed abdomen, may lead to a diagnosis of bronchial spasm.

I have found this sign both useful and reassuring. It fails to appear only when there is simultaneous and complete central respiratory depression.

Emergence from respiratory arrest due to central respiratory depression is first indicated by another sign.

Gentle handling of the bag will elicit a point at which the very lightest compression initiates a slow but full diaphragmatic contraction followed again by respiratory inactivity until another gentle touch on the bag again causes a further diaphragmatic contraction. After a few repetitions of this manœuvre spontaneous respiration returns. The feeling in eliciting this response is of toppling over a very finely balanced mass by the lightest touch; and I have named this sign the "trigger response" because the lightest touch sets it off. I have elicited it during emergence from the depression caused by both thiopentone and pethidine. For some reason, for which I am unable to account, it is more readily and constantly elicited in the emergence from depression due to thiopentone.

If this response is caused, as it would seem to be, by stimulation of the stretch receptors in the lungs, it would appear to be a reversal of the Hering-Breuer reflex by which stimulation of the stretch receptors terminates the act of inspiration and initiates expiration. Furthermore, since the separate central respiratory centres are depressed in the reverse order of their evolution, and recover in the order of their evolution, may it not be that this "trigger response" represents the most primitive of the respiratory reflexes; and, if this is so, may not the stimulus of the atmospheric pressure acting, through the open mouth, on the stretch receptors of the infant's lungs play an important part in initiating respiration in the newborn?

To modern methods of anæsthesia have been sacrificed one by one the cherished signs of anæsthesia, by which we used to teach the art and upon which we relied to pilot our patients through rough waters to safety. To the onlooker the plight of the patient, completely paralysed and apnœic, with pulse-rate disrupted by gallamine and the blood-pressure "controlled" at some near-catastrophic level, must seem extreme. Electroencephalography will perhaps come to be our Radar; but meanwhile these two signs may prove useful. By their help I have been able to determine the nature of respiratory arrest; and with unduly prolonged arrest the final emergence of the "trigger response" has almost invariably pointed to thiopentone as the causative agent.

Bournemouth. S. F. DURRANS.

CURE OF TOBACCO-SMOKING

SIR,—I suggest that the gist of Dr. Lennox Johnston's article last week can be expressed in a few words:

Smoking is a modern social habit; it is expensive, and not obviously detrimental to health. The habit can quite easily be broken by the exercise of a small amount of self-control, provided that there is a real desire to stop smoking.

I have yet to find the smoker who is an addict in the sense that a drug-taker is an addict, or the smoker who has been adversely affected in bodily or mental health when through force of circumstances tobacco has been denied to him.

I would suggest that smokers who fail to give up the habit after they have been advised to do so, or have expressed some intention of so doing, invariably have no real intention of abstaining. In my experience the provident man or woman who finds smoking too expensive a luxury, and definitely decides to stop the habit, always succeeds without great difficulty.

Louth, Lincolnshire. E. C. CORDEAUX.

SIR,—Dr. Johnston has given one account of the effects of giving up smoking. Let me, from a much shorter experience of abstinence, give another.

For thirty years I smoked heavily. The threat of lung carcinoma affected me not at all; I would willingly risk that possibility to continue to have the pleasure and comfort of smoking. But about six weeks ago I decided, for financial reasons, to stop smoking.

Instead of a "sustained uplift of spirits and of general interest" I have been morose, irritable, and unable to concentrate. Time hangs heavily on my hands, I have lost interest in my work and my hobbies, and I have nothing to look forward to. I have acquired an enormous appetite which is impossible to satisfy, and a great increase in flatulence and flatus. I have become lazy and depressed, and only my sexual potency, of which I had no complaints, remains unaffected.

Until I read your contributor's article I was well content not to touch my many comforting pipes. Since reading it my resolve has weakened, and I can see no reasonable future without tobacco.

TEMPORARY NON-SMOKER.

PS.—My colleagues disagree with this and say that at work I am much better tempered.

SIR,—Dr. Lennox Johnston, in his erudite paper, has told us everything about tobacco-smoking, except the cure.

Vague psychotherapy, in which the physician has to be patient (and the poor victim more so), reinforced by the induction of a cancerphobia, is, in my opinion, unlikely to overcome the habit. Dr. Johnston has, however, illustrated the suggestive element of smoking, and this, I believe, provides the answer. About 50% of people can be cured of the smoke habit by simple suggestion, used rapidly, under varying degrees of hypnosis, and the figures are higher if hypnotherapy and re-education are used.

Prince of Wales's General Hospital, London, N.15. GORDON AMBROSE.

SIR,—I found Dr. Lennox Johnston's article more interesting as an account of the development and perpetuation of the tobacco habit than helpful to those desirous of emancipating themselves. He touches on all the relevant points under "how to stop smoking," but in my view does not sufficiently emphasise auto-suggestion.

Before going to sleep one should think of smoking as an unnecessary, expensive, somewhat offensive, and physically deleterious habit. One should concentrate on the obvious disadvantages of smoking—such as irritation to the respiratory passages, eyes, and tongue, interference with appetite, staining of teeth and fingers, risk of damage to the eyes from hot particles of ash while driving, the destruction caused to paint work and carpets by careless guests, the pollution of the consulting-room atmosphere by nervous patients and colleagues who chain smoke, and so on.

Some effects of smoking are more resented than others; so the patient is advised to concentrate on those aspects of the habit which particularly annoy or repel him, and these should constitute his main auto-suggestive theme. After a few sessions of counter-suggestion the smoker finds his cigarettes less enjoyable, and within a matter of days will be smoking less and more frequently refusing the offer of cigarettes from others.

He does not require to be adamant about giving up smoking but should just set about altering his attitude towards the habit. He should continue to carry cigarettes but should endeavour to remember to ask himself if he really wants one before actually lighting up.

The object is to develop an awareness of the desire to smoke and then to elect to have a cigarette or not. Even if one fails to achieve this awareness, the distaste for cigarettes, which is inevitable after a period of counter-suggestion to smoking, may enable one to bring the habit well into consciousness. At that point the decision to continue the cigarette or not can be made.

I do not agree with Dr. Johnston that "it is necessary to do much more than merely decide to give up smoking." One can start to toy with the idea of giving it up. One need not forswear smoking. The greater the determination to abandon the habit the more the desire for a smoke is made conscious and the law of reverse effort operates—i.e., the harder one tries the less one succeeds. Why try so hard? The habit should not be given so much importance. If one decides to give it up one should proceed with the ritual of auto-suggestion which will bring the habit into consciousness. It is a habit which is much more readily abandoned than is commonly appreciated. I entirely agree with Dr. Johnston that smoking is harmful. "Is smoking bad for one?" should always be answered with an unequivocal "yes."

London, W.1. ELLIS STUNGO.

WHAT OF GENERAL PRACTICE?

SIR,—Your leading article of Sept. 6 states:

"The medical student, trained in scientific method, naturally measures the general practitioner's opportunities by the precise yardstick of science—and shakes his head. What may escape him is that the good family doctor laces science's cold portion with the warmer stuff of humanism. Some of this humanism is being formalised in the doctrine of social medicine, which is finding its way into curricula; but, even so, the general practitioner's twofold technique remains essentially empirical, . . . Dons, especially those who pursue scientific disciplines, are not remarkable for their tolerance of the empirical."

This seems to imply that science and empiricism are antitheses and that science must be inhuman. According to the *Concise Oxford Dictionary* empiric means "based, acting, on observation and experiment, not on theory." Excellent examples of empirical studies are, therefore, provided by those numerous controlled experiments which demonstrate the value, or lack of value, of drugs, and which are such a feature of modern medicine. The antithesis of empiricism is doctrine based on theory alone, and much medical treatment of the past, and even of the present, rested on such a basis. Our forefathers performed phlebotomy to get rid of the phlegma which could be seen when the patient's blood was allowed to stand; they starved the feverish patient to prevent the fires of his fever burning more fiercely; and they purged people to rid them of noxious matters. We refrain from giving lettuce to the subjects of peptic ulcer, because lettuce leaves will erode the ulcer; we make dropsical patients thirsty because we deduce that if we allow them to drink freely their dropsy will increase; and we still give freely—or at least are advised to do so in the very latest articles—brisk purges to the subjects of innumerable conditions, from boils to acute tonsillitis, to minimise their toxæmia. And witchdoctors mutter

imprecations and go through elaborate ceremonial to get rid of the evil spirits which are responsible for the patient's illness. Is it then to be supposed that these remedies are scientific, and that giving penicillin (the belief in the value of which is based on innumerable observations on mankind) is not scientific? No-one, of course, adopts such a view, and all would agree that controlled experiments to illustrate the value of drugs are scientific. But it is still commonly believed that the use of remedies depending solely on theory is scientific; in fact such remedies should always be suspect.

So far from his technique being "essentially empirical," the general practitioner is at a disadvantage by comparison with those who work in hospitals because it is difficult for him to make sound empirical observations. The general practitioner who says he is convinced that a tonic has benefited a patient is making unjustified deductions from his observations; all he should deduce legitimately is that the patient has apparently improved over the period in which he has taken the tonic. To assess the value of the tonic requires a large series of similar cases, half of whom are given the tonic and the other half an inert but similar-looking preparation, and all of whom are questioned closely and consistently. The general practitioner can hardly perform an investigation of this kind, and he has to depend on the empirical observations of others.

The view in your leading article that science is inevitably inhuman suggests that a doctor is being scientific when he looks at a patient with numerous persistent complaints and profound personal problems from a purely organic angle—as a conglomeration of organs, disease of which must either be identified or excluded by means of a large number of investigations with expensive apparatus. And if in the end disease is excluded, he concludes that the patient must have "nothing the matter." But why should such a performance be called scientific? It is certainly folly, and it is strange that folly should be given the name of science.

Farnham, Surrey. JOHN W. TODD.

PARACOLON BACILLUS SEPTICÆMIA

SIR,—Dr. Kernohan's[1] account of this disorder reminds me of a similar case I saw earlier this year.

A man, aged 52, was admitted to hospital on Feb. 25 after moderate hæmatemesis that morning. He gave a history of two previous hæmatemeses, the last one, in 1947, being definitely preceded by ingestion of aspirin tablets for lumbago. On this occasion, he had had "gastric influenza," with anorexia, malaise, nausea, and retching for the previous 10 days; and the day before admission he had taken some brandy and aspirins. He had had no dyspepsia.

He was moderately febrile (100°F) but there were no signs of recent severe blood-loss (blood-pressure 110/70 mm. Hg, Hb 110%). There were no abnormal physical findings except for a very furred tongue and moderate abdominal distension. Expectant treatment was adopted.

Next morning his temperature had risen to 102°F, and it remained at this level until next day (Feb. 27) when the pulse-rate fell to 66 per min (Faget's sign). Enteric fever was now seriously considered, and was suggested further by absolute constipation for 5 days past, tympanites, and increased lethargy with absence of physical signs in the chest or elsewhere. There was no splenomegaly, but there were several faint dusky "rose red" spots on the trunk.

On Feb. 28 the white blood-cell count was 4300 per c.m. (polymorphs 36%, lymphocytes 61%) and next day 4600 (polymorphs 40%, lymphocytes 40%, monocytes 18%, eosinophils 2%); erythrocyte-sedimentation rate 3 mm. in 1st hr. (Westergren). Blood-culture was sterile after 3 days, but confirmatory evidence of a septicæmia was obtained from the urine and stools, which yielded a non-lactose-fermenting gram-negative bacillus, identified provisionally as *Salmonella paratyphi B* by agglutination, but by the Salmonella Reference Laboratory as a paracolon bacillus.

With treatment by chloramphenicol the patient's temperature fell and his general condition improved dramatically. He was discharged fit on March 17.

It was thought that this patient's hæmatemesis had resulted from gastric irritation produced by aspirin, together with increased gastric vascularity associated with gastritis due to infection with paracolon bacillus.

I should like to thank Dr. R. B. Niven for permission to publish this case.

Winchester. P. G. CRONK.

1. Kernohan, R. J. *Lancet*, 1952, i, 1090.

EMPLOYMENT OF REGISTRARS

SIR,—At a meeting of the consultants and specialists of the Bromley group, held on July 31, the proposals for the employment of senior registrars (including the exchange scheme) and registrars as agreed between the regional hospital board and the teaching hospitals were considered.

The meeting was very concerned to learn that it had been laid down that all candidates for the position of senior registrar must have held the post of registrar in a teaching hospital for 2 years. If this was correct it seemed clear that registrarships in non-teaching hospitals would be "dead-end" jobs, that there might very soon be difficulty in filling such posts at all, and that candidates for such posts would be of a poorer type than formerly, with the inevitable result that the health service would suffer.

The following resolution was therefore unanimously passed:

(*a*) That a strong protest should be made against the decision that candidates for the post of senior registrar must previously have held the post of registrar in a teaching hospital for 2 years.

(*b*) That the present proposal that of senior registrars should be selected entirely from the registrars of teaching hospitals would mean that doctors applying for registrarships in non-teaching hospitals would be of a poorer type than formerly, and that the health service would inevitably suffer as a consequence.

(*c*) That senior registrarships and registrarships should both be interchangeable between teaching and non-teaching hospitals.

RUFUS C. THOMAS
Acting Chairman.
A. C. GLENDINNING
D. P. VAN MEURS
Acting Secretaries.

SALT-LOSING NEPHRITIS

SIR,—Recently attention has been drawn to a phase or type of nephritis in which loss of salt in the urine is a prominent feature. In your issue of Sept. 6 Dr. Joiner and Dr. Thorne describe 3 cases in which this diagnosis was made. A second possibility present in 2 of their cases is that the salt loss was related to the presence of pulmonary tuberculosis.

Westwater et. al.[1] found the serum-sodium to be less than 137 m.eq. per litre in 55 out of 169 cases of pulmonary tuberculosis admitted to a sanatorium. 21 of these cases came to autopsy, and, apart from amyloid disease in 1 instance, no renal disorder was discovered. These patients had weakness, skin pigmentation, hypotension, diarrhœa, and vomiting, many of which symptoms occurred in the cases described by Dr. Joiner and Dr. Thorne.

Furthermore we cannot agree that their second case showed chloride depletion, whether the levels are taken in milligrammes per 100 ml. or in milli-equivalents per litre (the values given do not appear to correspond). The diagnosis in their third case would appear to be based solely upon a single serum-sodium level of 131 m.eq. per litre, which was obtained after a period of eight days in which added salt was excluded from the diet. In a

1. Westwater, J. O. Stiven, D. Garry, R. C. *Clin. Sci.* **4**, 73.

patient with chronic nephritis some fall in the serum-sodium level might be expected to occur.

Evidence of long-standing pyelonephritis is a not infrequent finding at autopsy; and in our view the presence of active pulmonary tuberculosis is more likely to account for the salt loss in cases one and two. In case three the evidence of salt loss submitted seems insufficient for it to be included in the group with excessive loss of salt in the urine.

University College Hospital, London, W.C.1. M. ATKINSON
T. A. J. PRANKERD.

MALARIAL FEVER THERAPY

SIR,—The article by Mr. Shute (Aug. 16) draws attention to an undesirable practice. This states that malarial infection by intramuscular inoculation of whole blood is an alternative to the technique of using parasites.

As one who has witnessed the tragedies of hæmolytic disease of the newborn, and transfusion morbidity, from untimely disregard for the known facts of Rh sensitisation, I would ask the Malaria Reference Laboratory to bear in mind the inadvisability of using this method to infect girls and also women of the child-bearing years. If the method is to be retained, then due regard should be paid to the possibility of such sensitisation.

Uxbridge, Middlesex. JOHN PRICE.

DEFORMING FACTORS IN POLIOMYELITIS

SIR,—I have read with great interest Mr. Mitchell's analysis last week of "muscle spasm" and allied disorders and also the treatment he advised in his earlier communication.[1]

In this connection I feel that we should report some recent experiences in the treatment of acute poliomyelitis at Stoke Mandeville Hospital isolation block, where, during the present outbreak of the disease, we have had the benefit of the services of a nurse trained at St. Thomas's Hospital who has recently studied poliomyelitis in the U.S.A.

This experience has led us to institute very frequent passive movements with gentle stretching of tight muscles, and frequent changes of position in bed, from the first day of the disease. The physiotherapist treats the patient once a day, but on at least five other occasions in each 24 hours passive movements are carried out by the nurse, who is trained to do them. In addition the posture of the patient in bed is changed on about ten occasions during the 24 hours, the supine, lateral, semi-prone, and prone positions all being used. This plan gets rid of most muscle tightness within 2–3 weeks, and seems to be entirely satisfactory in practice. The nursing methods used could be demonstrated to a limited number on application to the Matron, Stoke Mandeville Hospital, Aylesbury, Buckinghamshire.

Department of Neurology, Radcliffe Infirmary, Oxford. W. RITCHIE RUSSELL.

Diary of the Week

SEPT. 14 TO 20

Wednesday, 17th

ROYAL EYE HOSPITAL, St. George's Circus, S.E.1
5.30 P.M. Mr. Howard Reed: Keratome and Scissors for Cataract Incision.

Friday, 19th

RENAL ASSOCIATION
4.30 P.M. (41, Portland Place, W.1). Prof. J. G. G. Borst (Amsterdam): Electrolyte and Water Balance with Relation to the Kidney.

BIOCHEMICAL SOCIETY
11 A.M. (The University, Glasgow). Scientific papers (opening of two-day meeting).

Saturday, 20th

INSTITUTE OF LARYNGOLOGY, 330, Gray's Inn Road, W.C.1
11 A.M. Dr. Stacey R. Guild (Baltimore): Recent Research in Otology.

1. *Brit. med. J.* 1952, 1, 649.

Public Health

Neglecting the Countryman?

IN his report for 1951, Dr. D. P. Lambert, divisional medical officer for the North Craven division of the West Riding of Yorkshire, says:

"Country folk are becoming increasingly conscious that most of the benefits of the Welfare State are concentrated in the cities, and . . . it is felt that some things could and should be better shared. Medical services are especially wished for; and the demand for mobile clinics and for mobile consultation facilities increases each year. For major surgery and for prolonged medical investigation patients will always have to go to the big hospital centres; but there is a great deal of diagnostic work . . . that could be as well done in a mobile clinic as in a hospital outpatient department."

Infectious Diseases in England and Wales

Disease	Week ended August				
	2	9	16	23	30*
Diphtheria	19	19	17	23	22
Dysentery	93	119	125	119	90
Encephalitis:					
Infective	7	2	9	2	7
Postinfectious	1	2	2	1	1
Food-poisoning	164	150	146	190	139
Measles, excluding rubella	7310	7012	6099	5256	3649
Meningococcal infection	20	18	35	29	28
Ophthalmia neonatorum	34	19	34	39	28
Paratyphoid fever	130	63	40	58	44
Pneumonia, primary or influenzal	229	239	247	207	220
Poliomyelitis:					
Paralytic	139	167	170	153	150
Non-paralytic	91	83	88	68	65
Puerperal pyrexia and fever	228	242	242	244	216
Scarlet fever	999	722	643	559	557
Smallpox	—	—	—	—	—
Typhoid fever	5	4	4	13	4
Whooping-cough	2045	1766	1872	1806	1861

* Not including late returns.

Appointments

CONNOLLY, M. R., L.R.C.P.E.: first asst., anæsthetic department, Royal Free Hospital, London.
SALMON, L. F. W., M.B.E., M.S. Lond., F.R.C.S.: consultant ear, nose, and throat surgeon, Guy's/Evelina Hospitals, London.
STEPHENS, J. P., M.B. Camb., F.R.C.S.: senior surgical registrar, Norfolk and Norwich Hospital.
SUMMERS, H. A. H., M.B. Belf., D.P.H.: asst. county M.O.H. and district M.O.H., borough of Daventry and the rural districts of Daventry and Brixworth.

Colonial Service:

BIRD, A., M.D.: M.O., Windward Islands.
BURY, E. J., M.R.C.S., D.P.H.: D.D.M.S., western region, Nigeria.
CHARLES, E. D. B., M.D. McGill, M.P.H.: M.O.H., Jamaica.
COHEN, R. I., M.B. Lpool, F.R.C.S.: M.O., South Pacific Health Service.
DIDSBURY, BRIAN, M.B. Manc.: M.O., Malaya.
GOULDING, M. D., M.B.: M.O., Federation of Malaya.
HARRIES, J. R., M.B. Lond., M.R.C.P., D.C.H.: M.O. (special grade), Kenya.
HARRIS, B. P., M.A., M.D. Camb., D.T.M.&H.: senior M.O., Kenya.
HODGES, W. A. A., B.A., M.B. Camb., F.R.C.S.: M.O. (special grade), Tanganyika.
PARK, ROBERT, M.R.C.S.: senior M.O., Nyasaland.
PASQUAL, R. S. H., M.B. Edin.: M.O., Kenya.
REID, H. A., M.B. Edin., M.R.C.P.E., D.T.M.&H.: specialist physician, Malaya.
SEXTON, J. P., M.B. Edin., D.P.H.: regional senior health officer, northern region of Nigeria.
SINCLAIR-HALL, A. H., M.D. Manc., F.R.C.S.: senior specialist, Nigeria.
VERLEY, DORIS, M.B. Edin., D.A.: medical specialist (anæsthetist), Jamaica.
WATERS, I. R., M.R.C.S.: M.O., Nyasaland.
WELLS, R. H. C., M.B. Lond.: M.O., Federation of Malaya.

Manchester Regional Hospital Board:

CALDER, A. G. S., M.B. Edin., F.R.C.S.E.: consultant E.N.T. surgeon, Wigan and Leigh Hospitals.
DARK, J. F., M.B. Manc., F.R.C.S.: consultant thoracic surgeon, Baguley and Park Hospital, Manchester.
JACK, G. D., M.B. Edin., F.R.C.S.: consultant thoracic surgeon, Baguley and Park Hospital, Manchester.
PARKER, R. P., M.B. St. And.: asst. anæsthetist, Burnley and district hospitals.

The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

Notes and News

ROYAL MEDICAL BENEVOLENT FUND

DURING 1951 the Royal Medical Benevolent Fund helped 88 new applicants, and the number of its beneficiaries is now over 600. Reporting on the year, Dr. R. Cove-Smith, the hon. secretary, says that during the year £41,467 was disbursed, including £21,865 in grants, £10,609 in annuities, £2028 as Christmas gifts, and £2020 as New Year gifts. Working expenses amounted to 6·6%. Investment income was £13,794 and subscription income £24,410; income-tax recovered under covenants totalled £5810. In addition, £18,114 was received in legacies and credited, as usual, to capital account. Dr. Cove-Smith observes that, with income-tax at 9*s*. 6*d*. in the pound, each guinea of covenant subscriptions represents an income of £2 to the Fund; and he asks all supporters to consider this method of subscription. The headquarters of the Fund are at 1, Balliol House, Manor Fields, Putney, London, S.W.15.

A NEW KIND OF CECIL HOUSE

WOMEN wandering about the streets of London in search of a cheap lodging are fortunately no longer as common as they were in 1925, when Mrs. Cecil Chesterton set out, with nothing in her pockets, to see what it felt like to be one of them. But there are still more than enough of them to disturb our peace of mind if we stop to think about it. The Cecil Houses, which she founded, still fill themselves every night, and the numbers turned away do not diminish. Those who get there in time can still get a clean and comfortable bed, a hot bath, and facilities for washing clothes, for a sum which has risen, with the change in the value of money, from 1*s*. to 2*s*. 3*d*.; a cot for a baby costs an additional 3*d*. They are asked no questions; they want, and are paying for, a night's lodging, and their private lives are respected. The only stipulation made is that they shall be sober.

Over the course of the years six Cecil Lodging Houses have been opened; some were closed for a time by bombing, and have since reopened—all but one, which is let temporarily for light industry until it can be rebuilt. In 1938 a new kind of Cecil House was opened—a residential club, in Gower Street, for 72 working girls who pay £2 a week, and must not be earning more than £5. This building was let during the war to the Canadian Legion but has been fulfilling its original purpose since 1947. Next year another new venture is to be launched—a residential club for 72 old ladies. The building is up, in Medlake Street, North Kensington; and it is delightful, from the roof garden and verandahs, and the nineteen dormitories, to the comfortable common-rooms, the convenient kitchen, and the central-heating installation in the basement.

Once launched, the Cecil Houses pay their way, and the new residential home will be no exception; but it has cost £65,000 to buy the site and build on it, and not all of this sum has been collected yet. Those who wish to contribute should send their subscriptions to the Hon. Treasurer, Cecil Houses (Inc.), 193, Gower Street, London, N.W.1.

A VOICE FROM THE PAST

Daniel Drake was born in New Jersey in 1785. At the age of 2 he took part in the migration to the western parts of the United States. In the turmoil of those pioneer days a boy's education was apt to be neglected, but Daniel was soon able to take the matter in his own hands; for, as he later wrote, "I could read and examine a dictionary for the meaning of words and here is the starting point of all improvement." And improvement thus started led to his apprenticeship at 15 with a doctor in Cincinnati, and carried him on to a place of distinction in the history of American medicine. He became a physician, teacher, and writer whose reputation spread far beyond the Ohio Valley where he spent most of his life.

Biographical facts, however impressive, give a poor picture of the man, but his written words do much to fill in the details—and Dr. Drake was a vigorous and prolific writer. His essays on medical education and the medical profession, first published in 1832, have now been reprinted.[1] Many of his pungent criticisms must have been unpopular at the time, and indeed some of them may touch a sore spot here and there even now. "The profession abounds in students and practitioners who are radically defective in spelling, grammar, etymology, descriptive geography, arithmetic, . . . and book-keeping." He also demanded "a competent knowledge of the elements of physical geography, general history, the art of composition, algebra, geometry, and mechanics." How his students must have quailed! He deals as devastatingly with the failings that he detected in the medical schools of the time; and his ideas on a proper medical training laid the foundations of modern American teaching methods. He wrote so entertainingly that he should be read again even if his lessons had all been learnt, which is by no means the case.

1. Practical Essays on Medical Education and the Medical Profession in the United States. By DANIEL DRAKE, M.D. Baltimore: Johns Hopkins Press. London: Oxford University Press. 1952. Pp. 103. 20*s*.

THE WORKS OF SIR ALMROTH WRIGHT

Dr. Leonard Colebrook, F.R.S., loving disciple of an unusual man, has prepared a bibliography of all the published works of Sir Almroth Wright,[1] and has appended to each title a short account of the contents. Most of these deal with immunisation, Wright's major interest, and it is impressive to see the vast field he ranged and the notable contributions he made to this subject. Two works on which Dr. Colebrook evidently sets a high value are *Prolegomena to the Logic which searches for the Truth*, and *Alethetropic Logic* (still unpublished) to which the *Prolegomena* was written as a foreword. The main work began to take shape, Dr. Colebrook says, in the 'nineties, when Wright had become interested in the physiological processes associated with emotional disturbances. This led him to reflect on the nature of belief, and the intellectual operations usually included in the word "logic." "It seemed to him that the modern development of psychology and physiology called for a new system of logic—one which was not concerned only with Reasoning, but took account also of all the processes by which we arrive at our Beliefs." Three contributions, whose shocking illiberality nowadays raises a smile, are concerned with the case against woman suffrage; perhaps it would have been kinder to leave them out.

SAFETY FOOTWEAR

IN industry injuries to the feet are a common cause of disablement. The Ministry of National Insurance found that in 1949 and 1950 such injuries accounted for about 4% of all successful claims for injury benefit. The British Standards Institution, in coöperation with other organisations, has issued a standard for men's safety boots and shoes (B.S. 1870/1952, price 2*s*. 6*d*.). Shoes made by this standard, which were demonstrated in London this week, have an external or internal steel toecap, weighing 2 oz. and designed to withstand a shock test of 150 foot-lb. or a dead weight of 3 tons.

Royal Medico-Psychological Association

Dr. W. Rees Thomas will deliver the Maudsley lecture to this association on Thursday, Nov. 6, at 2.15 P.M., at 1, Wimpole Street, London, W.1. He is to speak on The Unwilling Patient.

London Hospital

On Thursday, Oct. 9, at 4.15 P.M., at the Medical College, Prof. S. P. Bedson, F.R.S., will deliver the Schorstein lecture on Twenty-five Years' Progress in Virus Research.

Royal Free Hospital

Sir Henry Dale, O.M., F.R.S., will deliver the opening address of the 1952–53 session to the medical school on Friday, Oct. 3, at the Senate House, University of London, W.C.1, at 3 P.M.

Guy's Hospital

The biennial dinner for past medical and dental students will be held in the Connaught Rooms, Great Queen Street, London, W.C.2, on Friday, Oct. 3, at 7.30 p.m. Tickets (25*s*. exclusive of wines) are obtainable from Mr. O. Gayer Morgan, hon. secretary of the dinner, Medical School, Guy's Hospital, London, S.E.1.

Westminster Medical School

On Monday, Oct. 6, at 3.45 P.M. at Church House, Great Smith Street, S.W.1, Sir Raymond Evershed, P.C., the Master of the Rolls, will give the inaugural address.

1. Bibliography of the Published Writings of Sir Almroth Wright, M.D., F.R.S. London: Heinemann. 1952. Pp. 32. 6*s*.

Society of Chemical Industry

On Monday, Oct. 20, at 5.30 P.M., at the rooms of the Chemical Society, Burlington House, London, W.1, at a meeting of the crop protection panel of the agriculture group, Dr. J. M. Barnes will speak on Health Hazards in Crop Protection.

Rubber Products for Hospital Use

With the collaboration of the professional and industrial interests concerned, the British Standards Institution is preparing a series of standards for rubber products used in surgical and hospital practice, and the following have now been published :

B.S.1803—Surgical rubber gloves (price 1*s.* 6*d.*) deals with gloves made by dipping in rubber solution (both cold and hot vulcanised), or by dipping in latex. Recommendations are given for storing and sterilisation.

B.S.1883—Rubber ward-dressing gloves and porters' gloves (2*s.*) covers three types of gloves—namely, rubber-solution dipped, rubber-latex dipped, and those built up from sheet rubber. Methods of marking to show date of manufacture are laid down.

B.S.1884—Rubber post-mortem gloves (2*s.*) is similar in scope to B.S.1883.

B.S.1882—Rubber tubing for hospital use (2*s.*) includes specifications for pressure, drainage, stethoscope, and Paul's tubing. Transfusion tubing is still under consideration, and will be dealt with by an amendment slip to the present standard as soon as the work is completed. Exact methods of manufacture, with dimensions and tolerances, are specified, and details are given of physical tests to ensure that the quality of rubber used is satisfactory for each purpose.

Copies of these standards may be had from the sales branch of the Institution, 24, Victoria Street, London, S.W.1.

British Legion Homes

This year the British Legion has completed its post-war plan to provide 8 special homes. The 4 country homes for the aged at Westgate, Cromer, Ripon, and Bwlch, near Brecon, accommodate 220 men and women, 130 of whom are disabled. Every year more than 3000 men and women spend a fortnight at the convalescent homes at Southport, Weston-super-Mare, Sevenoaks, and Helen's Bay in Northern Ireland.

Institute of Child Health, London

Ten postgraduate lectures on Disease in the Young Animal and the Child are to be given at the Hospital for Sick Children, Great Ormond Street. The lectures will be held on Mondays, at 5.30 P.M., beginning on Oct. 13. Further particulars may be had from the secretary of the institute, Great Ormond Street, W.C.1.

Wessex Rahere Club

The autumn dinner of this club will take place at the Grand Spa Hotel, Clifton, Bristol, on Saturday, Oct. 25. Membership of the club is open to all Barts men practising in the West Country. Further details may be had from Mr. A. Daunt Bateman, the hon. secretary, 3, The Circus, Bath.

Vellore Christian Medical College, South India

Friends of Vellore are to hold their annual reunion on Wednesday, Oct. 8, at Caxton Hall, Westminster, S.W.1, at 3.30 P.M. The speakers will include : Dr. Margaret Brand, Mr. Paul Brand, Dr. Gwenda Lewis, and Dr. P. Koshy.

Association of Clinical Pathologists

The annual general meeting of this association will be held at the Westminster Hospital Medical School, London, S.W.1, from Oct. 2 to 4.

Hunterian Society

The annual party of this society is to be held at 41, Portland Place, London, W.1, on Thursday, Oct. 2, at 6 P.M., when recent additions to the museum will be shown.

Rations for Patients with Cœliac Disease

A new category of extra rations has been introduced for children with cœliac disease. In future children who are being treated on a wheat- or gluten-free diet may be allowed one extra ration of fats (butter, margarine, and cooking-fat), one extra meat ration, and one priority allocation of eggs a week. These allowances are alternative to, and not additional to, the extra rations at present granted. Medical certificates, in addition to providing the figures for a stool fat-analysis or fat-absorption test, should state that the patient is on a gluten-free diet. The Ministry of Food's medical advisers are prepared to give consideration to adults suffering from steatorrhœa who have been placed on a similar diet.

International Congress on Rheumatic Diseases

The eighth International Congress on Rheumatic Diseases will be held at Geneva from Aug. 24 to 28, 1953. The following subjects have been chosen for discussion : Connective Tissues and Rheumatism ; Steroids in the Treatment of Rheumatism ; the End-results of Surgery for the Rheumatic Hip ; and Occupational Reablement. Further particulars may be had from Prof. K.-M. Walthard, Institut de Physiatrie, Hôpital Cantonal, Geneva, Switzerland.

St. Thomas's Hospital

The old students' dinner will take place at the Trocadero Restaurant, Piccadilly Circus, London, W.1, on Friday, Oct. 17, at 7.30 P.M., when Mr. L. E. C. Norbury, will take the chair. Tickets (29*s.* exclusive of drinks) can be obtained from the hon. secretaries, G. A. MacGregor, R.A.P., and C. R. Savage, R.A.S., St. Thomas's Hospital, S.E.1.

Illuminating Engineering Society

On Jan. 28, Prof. E. D. Adrian, O.M., F.R.S., will deliver the Trotter-Paterson lecture to this society. He will speak on the Nervous Reactions of the Retina. Dr. W. J. Wellwood Ferguson will deliver the presidential address on Oct. 14. Both meetings will be held at the Royal Institution, Albemarle Street, London, W.1, at 6 P.M.

Newsholme Lectures

Prof. W. M. Frazer, medical officer of health for Liverpool, is to deliver these lectures at the University of London in 1954.

Mr. A. S. Parkes, D.SC., F.R.S., head of the division of experimental biology of the National Institute for Medical Research, Mill Hill, London, leaves on Sept. 17 for a lecture tour in Latin America, which has been arranged by the British Council.

The British Standards Institution has issued a draft British Standard for clinical maximum thermometers (B.S. CO[LBC] 3325), comments on which should be sent before Oct. 9 to the institution, 24, Victoria Street, London, S.W.1.

The Cambridge Instrument Company Ltd. are issuing to delegates at the European Congress of Cardiology a monograph on the *Development of the Electrocardiograph* by Mr. S. L. Barron, M.R.I., to which Sir Alan Drury, F.R.S., has contributed a foreword. Some additional copies are available, and will be sent, without charge, to doctors who apply to the company, 13, Grosvenor Place, London, S.W.1.

Births, Marriages, and Deaths

BIRTHS

ATKINSON.—On Sept. 1, at Bromley, Kent, to Mollie (née Morrisioe), wife of Mr. W. J. Atkinson, M.D., F.R.C.S.—a daughter.

CLARKE.—On Aug. 29, at the Purey Cust Nursing Home, York, to Catherine (née Waugh), wife of Mr. P. R. R. Clarke, F.R.C.S.—a son.

FELIX-DAVIES.—On Aug. 29, in London, to Joan (née Kellett), wife of Dr. D. Felix-Davies—a son.

HICKS.—On Sept. 3, at Edgware General Hospital, Edgware, to Marie, wife of Dr. Frederick N. Hicks—a daughter.

HIGHTON.—On Aug. 25, to Dr. Roberta Highton (née Baker), wife of Dr. Thomas C. Highton, M.R.C.P., of Rotorua, New Zealand—a son.

LOTHIAN.—On Aug. 31, at Shoreham, Kent, to Joan (née Hamlyn), wife of Dr. William Lothian—a son.

LUCAS.—On Aug. 25, at Princess Elizabeth Hospital, Nairobi, Kenya, to Dr. Shelagh Lucas (née Fair), wife of Mr. J. M. S. Lucas, M.R.C.V.S., Box 2141, Nairobi—a daughter.

MUNRO.—On Sept. 6, at Crayford, Kent, to Dr. Olive Munro, wife of Dr. Ian Munro—a daughter

ROBERTSON.—On Sept. 4, to Helen (née Preston), wife of Dr. James Robertson, 66, Gloucester Gardens, W.2—a son.

TASKER.—On July 25, at Northampton, to Anita, wife of Dr. J. R. Tasker—a son.

WOHL.—On Aug. 31, at the London Clinic, to Hilda (née Hoffman), wife of Dr. M. Wohl—a daughter.

MARRIAGES

DEVITT—BROWNLEE.—On Sept. 6, at Pinner, Herbert P.-S. Devitt, M.R.C.S., to Carol Brownlee.

DEATHS

ANDREWS.—On Sept. 2, at Gorse, Blatchington, Seaford, Henry Arthur Andrews, M.R.C.S., formerly of Tonbridge, aged 80.

INNES.—On Aug. 24, at Grantown-on-Spey, Inverness-shire, Flora Riddell Innes, M.B. Edin., formerly of the Christian Medical College, Vellore, S. India, and of Brisbane, Australia.

MCKIBBIN.—On Sept. 5, at his home, Frederick McKibbin, O.B.E., M.B. Belf., colonel, late R.A.M.C.

POLLARD.—On Sept. 3, at Pound Hill, Framfield, Sidney Pochin Pollard, M.D. Camb., F.R.C.S.

SMALL.—On Aug. 25, at his residence, Kinghurst, Stoke Gabriel, Devon, Robert Small, M.R.C.S., D.P.H., D.T.M., formerly M.O.H. Mombasa.

WARDROP.—On Aug. 30, at his home, 45, Northumberland Road, Leamington Spa, John Glen Wardrop, M.D. Lond., aged 63.

PREGNENOLONE B.D.H.

for oral administration in the treatment of

Rheumatoid arthritis

"*Sixty-four patients with rheumatoid arthritis were treated with pregnenolone by mouth in dosages averaging about 500 mg. daily, over varying periods of time ranging from two to thirty weeks. Twenty-four patients experienced striking improvement; 26 showed minor improvement; and 14 showed no improvement. The usual maintenance dose was 400 mg. daily. There was a great tendency to relapse after the medication was discontinued. There was a direct relationship between the length of time pregnenolone was administered and the length of time improvement was maintained after the medication was discontinued.*"

(THE JOURNAL OF CLINICAL ENDOCRINOLOGY, DECEMBER 1950, p. 1523.)

REDUCED PRICES: Pregnenolone B.D.H. is available as tablets each containing 100 mg. for oral administration. Bottles of 20 tablets 86/5. Bottles of 100 tablets 418/6. Solution for intramuscular injection. 100 mg. in 2.5 ml. ampoules. Boxes of 3 ampoules 16/8.

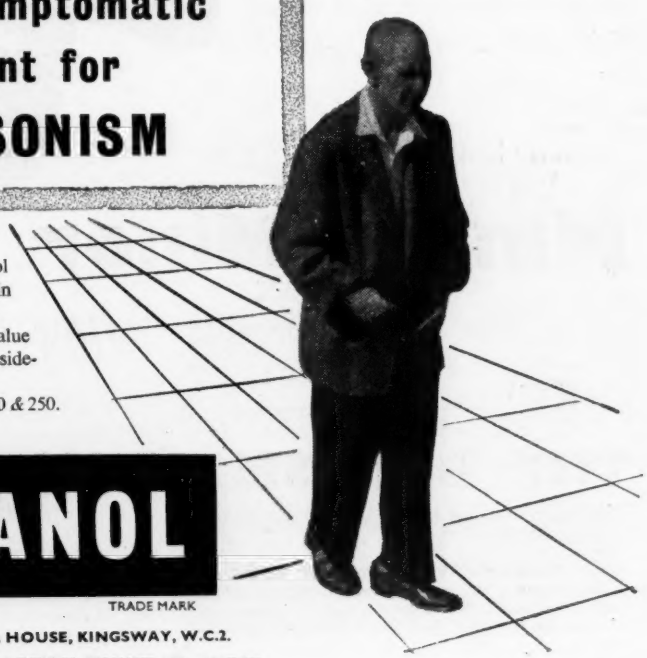
Prices in Great Britain to the Medical Profession

Further information is available on request to the Medical Department

THE BRITISH DRUG HOUSES LTD. LONDON N.1

Prnl/E/2a

Effective symptomatic treatment for PARKINSONISM



Trihexyphenidyl, also known as benzhexol hydrochloride, is now manufactured in Britain under the name '**PIPANOL**'.

Full-scale testing has indicated its value in all forms of Parkinsonism, while side-effects are negligible.

2 mgm. & 5 mgm. tablets. Packings of 100 & 250.

Please write for detailed literature

PIPANOL

TRADE MARK

BAYER **PRODUCTS LTD. AFRICA HOUSE, KINGSWAY, W.C.2.**

Associated Export Company: WINTHROP PRODUCTS LTD., LONDON

It takes a very speedy stork to get there before the Minnitt Minor—the lightest, most convenient gas/air analgesia apparatus in the world. Superbly constructed of strong, light materials, it actually weighs *less* than 13 lbs.—with filled cylinder! Ideal for emergency use, and as standard equipment for midwives, the Minnitt Minor gives a performance comparable with the existing well-known Minnitt range. Designed primarily for 50 gal. nitrous oxide cylinder. Approved by Central Midwives board.

Full particulars gladly supplied.

Minnitt Minor

The *Really* Portable Gas/Air Analgesia Equipment

THE BRITISH OXYGEN CO. LTD

MEDICAL DIVISION **LONDON & BRANCHES**

OVERSEAS: *Australia, Burma, Canada, Ceylon, East Africa, Egypt, Hong Kong, India, Malaya, New Zealand, Northern Rhodesia, Pakistan, Southern Rhodesia, South West Africa, Union of South Africa.*

Quinine

The well-tried and effective drug in the treatment of severe

Malaria

BRITISH JAVA CINCHONA GROWERS, 8/7 EASTCHEAP, LONDON, E.C.3.

WHEN YEAST IS INDICATED

DCL VITAMIN B_1

YEAST TABLETS

form a palatable and rich source of Vitamin B_1

The Dried Yeast from which these tablets are made contains in each gram approximately 300 International Units of Vitamin B_1, 50 micrograms of Riboflavin, 250-350 micrograms of Nicotinic Acid and 25-50 micrograms of Vitamin B_6.

★ *3 D.C.L. Vitamin B_1 Tablets equals 1 gram. Issued by all chemists in bottles of 50 and 100.*

ANOTHER QUALITY OF DRIED YEAST IN POWDER FORM IS AVAILABLE AS:—

DRIED YEAST (B.P.C.)

FOR HOME AND EXPORT

Full particulars may be obtained from

THE DISTILLERS CO. LTD.
12 TORPHICHEN STREET · EDINBURGH

R B C

Rybar Benzocaine Calamine Cream

A bland, sedative germicidal cream possessing powerful local anæsthetic properties. It is of great value in the treatment of eczematous conditions, pruritus, tinea and other skin infections due to bacteria or fungi. The soothing effect produced on the application of R.B.C. in cases of intractable itching materially assists healing by promoting sleep and preventing rubbing and scratching.

Formula:—

Phenylmercuric Nitrate	0.10%
Iso-butyl para-aminobenzoate	1.00%
N-butyl para-aminobenzoate	1.00%
Benzocaine	8.00%
Cholesterol	0.10%
Calamine	10.00%
Hydrophilic Base to	100.00%

All percentages w/w

Mode of issue: Collapsible tubes containing 1 oz.
May be freely prescribed on Form EC10.

Professional sample and literature on request from:

RYBAR *Laboratories* LTD.
TANKERTON · KENT

For the young patient who wishes to preserve her figure

Spirella

PROVIDES THE ANSWER

Because each garment is made to measure

For the patient whose figure needs supporting

Every female patient requires a supporting garment. More and more Doctors are telling their patients to look up the nearest Spirella Corsetiere in the Telephone Book.

The **SPIRELLA COMPANY OF GREAT BRITAIN LIMITED**
LETCHWORTH · HERTS Tel: Letchworth 159
AND SPIRELLA HOUSE · OXFORD CIRCUS · LONDON · W.1

Ingram's 'PERFEX' ENEMA ★ means perfection ★

Members of the medical profession recognize the "Perfex" Enema Syringe as a superior product of its kind. It is long-lasting because of the finest quality seamless rubber used in its construction. The "Perfex" has a perfect finish . . . is hygienic and easily kept like new. Complete with bone rectum pipe, rubber vagina pipe and leather shield, and packed neatly in an attractive box.

★ 100 YEARS OF EXPERIENCE ARE BEHIND INGRAM'S PRODUCTS

J. G. INGRAM & SON, LTD.
THE LONDON INDIA RUBBER WORKS
HACKNEY WICK, LONDON, E.9

The facts about Glucose

Glucose, a term used to include a substance resulting from the partial hydrolysis of starch, is in practice a general description rather than a precise one. It is applied to medical preparations which contain additives that may not always be wanted and to commercial products of varying degrees of refinement. To identify Glucose in its purest form, *and only in this form*, the term Dextrose is used.

Dextrose, as found in the blood and tissues, is the sugar into which the body converts all carbohydrates. Requiring neither digestion nor chemical alteration, Dextrose is used by the body as a source of immediate energy.

The Dextrose (pure medicinal Glucose) produced by the Pharmaceutical Division of Corn Products Company Limited is prepared in two convenient forms :—

Dextrosol Powdered Glucose

This contains no additives of any kind. It can be taken in large quantities without causing nausea, and should be prescribed in all cases where a patient needs a source of heat and energy with the least demand on the digestion. Packed in 1 lb. & ½ lb. cartons.

Dextrosol Karo Glucose Syrup

for Infants and Children

An appetising blend of pure Glucose and selected carbohydrates, carefully balanced to provide the ideal sugar addition to the milk diet of artificially-fed infants. Of special value in cases of nutritional disorder. Spread on rusks, bread, etc., it offers an excellent supplementary source of energy for growing children. Packed in 1 lb. tins. A Karo Baby Book is available for the guidance of mothers.

Professional samples of both Dextrosol products will be gladly provided. For further information, doctors are invited to write to the Dextrose Information Bureau, Wellington House, 125/130 Strand, London, W.C.2.

DEXTROSOL
BRAND

Glucose Products

are prepared by the Pharmaceutical Division of
CORN PRODUCTS COMPANY LIMITED
A Member of the Brown & Polson Group

A Diagnostic Set with Electric Head Lamp

This set contains the components of popular No. 3004 outfit, together with a Wickham Head Lamp which works from the battery handle. To assist in manipulating the various instruments, a useful extension handle (The Plandle) is provided. The Head Lamp uses an ordinary spotlight bulb which, with a carefully designed optical system, produces a brilliant patch of even illumination adjustable from 1 in. to 10 ins. in diameter. It is light and having a sponge rubber washable forehead pad is hygienic and very comfortable to wear. The Plandle facilitates the handling of separate components in awkward corners, by allowing the battery handle to be placed out of the way in the pocket or on the table.

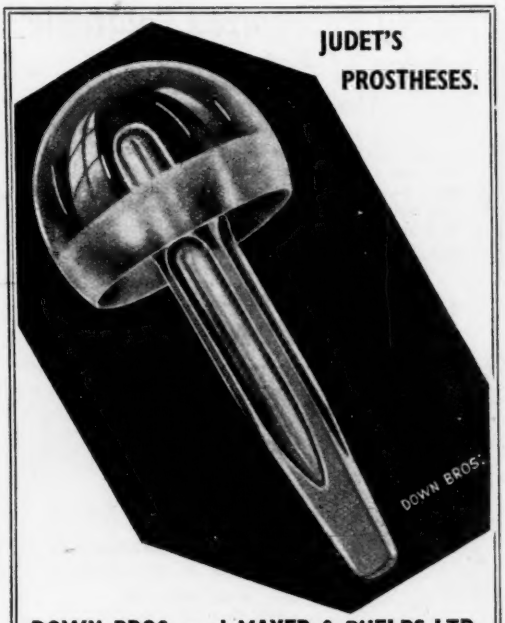
Set No. 3010 contains May Ophthalmoscope (which can be supplied with illuminated and magnified numbers if required), Auriscope with 3 Specula, Duplay Nasal Speculum, Bent Arm Throat Lamp with one each Laryngeal and Post-Nasal Mirrors, Flat Tongue Depressor, Plandle, Wickham Head Lamp, Large Battery Handle and Spare Lamp, complete in case. All components chromium plated and untarnishable.

Gowland
electric diagnostic instruments

OBTAINABLE FROM ALL SURGICAL SUPPLY HOUSES

Made near London, England, by a firm with half a century's experience of Surgical Instrument Manufacture.

JUDET'S PROSTHESES.



DOWN BROS. and MAYER & PHELPS LTD.
Surgical Instrument Makers
92-94, Borough High Street, London, S.E.1
and
32-34, New Cavendish Street, London, W.1

"LIVEROID"
Preparation of Liver

A concentrated preparation of the uncoagulated juice of liver, fortified with iron and glycerophosphates.

"LIVEROID" IS EMINENTLY SUITABLE FOR THE TREATMENT OF:—

Pernicious Anaemia and all forms of Megalocytic Anaemia characterised by a high colour index.
Normocytic or Secondary Anaemias due to loss of blood.
Microcytic Hypochromic Anaemias in which iron therapy combined with liver is desirable.
General Debility, Neurasthenia or weakness.

"LIVEROID" IS PLEASANT TO TAKE AND IS EASILY ADMINISTERED IN THE CORRECT DOSAGE

LITERATURE GLADLY FORWARDED UPON REQUEST

OXO LIMITED (Medical Dept.)
Thames House, Queen St. Place, London, E.C.4.
Phone: Central 9781

KH25

The **NEW** *Sharman's Kymographic Tubal Insufflation Apparatus*

This apparatus for recording a graph of insufflation has now been produced in an improved and simplified form. The whole control is now obtained by means of a single 4-position flow control valve instead of the two infinitely variable valves previously fitted. The two rates of flow available for insufflation are accurately pre-set during manufacture. The improved valve design ensures consistent operation over long periods. The CO_2 storage cylinder capacity is sufficient for a large number of operations without changing. Made with traditional care, finished in black leatherette with glossy grey instrument panels and supplied with a spare carbon dioxide cylinder and charts.

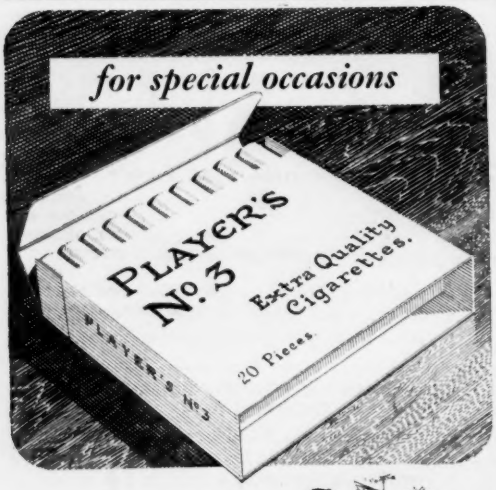
KH

KELVIN & HUGHES (INDUSTRIAL) LTD 2, CAXTON STREET, LONDON, S.W.1

110, BOTHWELL STREET, GLASGOW

---

for special occasions



PLAYER'S No 3

The Quality Cigarette

[3P 112A]

Newly Recognized Palatable Source of Potassium . . . .

The Neglected Mineral

Valentine's Meat Juice, with its high content of soluble potassium salts (equivalent to 74-97 mg. KCl per cc.) together with other inorganic salts, meat bases and small amounts of soluble proteins is a valuable dietary supplement, furnishing practical amounts of potassium in palatable form.

VALENTINE COMPANY, INC., RICHMOND, VA.

Valentine

Valentine's MEAT JUICE

VALITONE

Soluble BARBITONE gr. 2½, Stabilised VALERIAN m. 3, per drachm.

The economical and effective SEDATIVE & HYPNOTIC

4 oz. bottle 3/9
(also 40 oz. and 80 oz. sizes)

Samples on signed request

ROBERTS & CO.
76, New Bond Street, London, W.1

PRESCRIPTION for PRACTITIONERS

A Sickness Policy with the Medical Sickness Society

TAKE ONE NOW

For particulars please write to the Society
7 CAVENDISH SQUARE
LONDON, W.1 TELEPHONE: LANGHAM 2991

Round, fruity wine which has lain undisturbed in our cellars for fifteen years

1935 VINTAGE PORT

Corks branded "Vintage 1935
Bottled Coronation Year"

23/- per bottle 12/- per half-bottle

ARTHUR H. GODFREE & CO. LTD.
Founded 1814
11, ARUNDEL STREET, LONDON, W.C.2
Please write for our "Job Lots and Offers"

THE WORLD'S GREATEST BOOKSHOP

FOYLES
FOR BOOKS

Big new Medical Dept. now open

New, secondhand and rare Books on every subject.
Stock of over 3 million volumes.
Subscriptions taken for British, American and Continental medical magazines.
119-125 CHARING CROSS ROAD LONDON WC2
Gerrard 5660 (16 lines) ★ *Open 9-6 (inc. Sats.)*
Nearest Station: Tottenham Court Road

PROTECTIVE CLOTHING

SURGEONS' GOWNS with tie back and made from special lightweight unshrinkable cloth. All sizes.
Price 28/3

WHITE LONG COATS in single breasted style. Strong fully shrunk drill material. Three patch pockets. All sizes. **Price 25/10**

WHITE JACKETS. Strong drill, fully shrunk. Three patch pockets. All sizes.
Price 19/6

Postage and packing 1/- extra.
Write for latest price list.

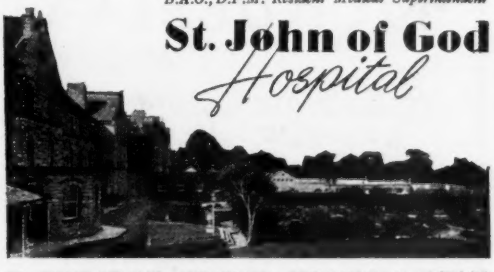
Charles Baker
& Co. Ltd.
137-138, TOTTENHAM COURT ROAD
LONDON, W.1.
Telephone: EUSton 4721/3

Mental and Nervous Disorders

● *Fully trained Nursing Staff of Brothers of St. John of God, Dietician, Resident Chaplain, Male Patients only. Terms on application.*

St. John of God Hospital is beautifully situated between the Dublin mountains and the sea, 5 miles from the city, and surrounded by its own pleasantly wooded and extensive grounds.
Every form of modern treatment. Electrical Convulsive Therapy (with Curare if necessary), Insulin Coma Unit, Modified Insulin, Prolonged Narcosis, Psycho-Therapy, Prefrontal Leucotomy, Occupational Therapy, Recreational Therapy, Staff of Regularly Visiting Consultants.

Address enquiries to: P.F. O'BRIEN, M.B., B.Ch. B.A.O., D.P.M. Resident Medical Superintendent



St. John of God Hospital

ST. JOHN OF GOD HOSPITAL, STILLORGAN, DUBLIN
Phone: 82043-855751

ST. ANDREW'S HOSPITAL

FOR NERVOUS AND MENTAL DISORDERS

NORTHAMPTON

PRESIDENT: THE EARL SPENCER

MEDICAL SUPERINTENDENT: THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

This Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders or who wish to prevent recurrent attacks of mental trouble: temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, biochemical, bacteriological, and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE

This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods; insulin treatment is available for suitable cases. It contains special departments for hydrotherapy by various methods, including Turkish and Russian baths, the prolonged immersion bath, Vichy Douche, Scotch Douche, Electrical baths, Plombières treatment, etc. There is an Operating Theatre, a Dental Surgery, an X-ray Room, an Ultraviolet Apparatus, and a Department for Diathermy and High-frequency treatment. It also contains Laboratories for biochemical, bacteriological, and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit growing.

BRYN-Y-NEUADD HALL

The seaside house of St. Andrew's Hospital is beautifully situated in a park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the North-West side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses, and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, etc.

For terms and further particulars apply to the Medical Superintendent (TELEPHONE: Northampton 4354 (3 lines)), who can be seen in London by appointment.

CAMBERWELL HOUSE, 33, Peckham Road, London, S.E.5

Telegrams: "PSYCHOLIA, LONDON"

A PRIVATE HOSPITAL FOR THE TREATMENT OF NERVOUS AND MENTAL DISORDERS

Telephone: RODNEY 4242 (2 lines)

Completely detached Villas for mild cases. Voluntary Patients received. Fifteen acres of grounds. Hard and grass tennis courts, putting greens, Recreation Hall with Badminton Court, and all indoor amusements. Occupational therapy, Calisthenics, Actinotherapy, prolonged immersion baths, shock and all modern forms of treatment. Chapel.

Senior Physician Dr. THOMAS T. BARTLETT, assisted by a resident Medical Staff and visiting Consultants

An Illustrated Prospectus giving fees, which are reasonable, may be obtained upon application to the Secretary

The Convalescent Branch is HOVE VILLA, BRIGHTON.

THE COTSWOLD SANATORIUM

On the Cotswold Hills, seven miles from Cheltenham, Stroud and Gloucester, equipped for the treatment of Pulmonary Tuberculosis. Full day and night nursing staff.

Terms from £10 per week

Full particulars from Secretary, COTSWOLD SANATORIUM, CRANHAM, GLOUCESTERSHIRE.

Telephone: Witcombe 2181

SPRINGFIELD HOUSE

Phone: BEDFORD 3417 **Near BEDFORD**

For MENTAL CASES (including the aged)

Fees from Eight Guineas per week (Separate Bedrooms for suitable cases without extra charge)

For forms of admission, &c., apply to the Resident Physician, CEDRIC W. BOWER.

INTERVIEWS IN LONDON BY APPOINTMENT.

HEIGHAM HALL, NORWICH

PRIVATE MENTAL HOME for Nervous and Mental illness. All types of treatment carried out. Accommodation for Alcoholics and Addicts available. Special Geriatric Unit now open. Fees from 6 gns. per week upwards according to requirements.

Apply to Dr. J. A. SMALL Telephone: Norwich 20080

CHISWICK HOUSE

PINNER, MIDDLESEX

Telephone: PINNER 234

A Private Home for the Treatment and Care of Mental and Nervous Illnesses in both Sexes.

A modern house, 12 miles from Marble Arch, in attractive secluded grounds. Patients treated under Certificate, Temporary or Voluntary status. Modern forms of treatment, including psychotherapy, narco-analysis, modified insulin, occupational therapy, E.C.T., etc. Fees from 12 guineas a week.

DOUGLAS MACAULAY, M.D., D.P.M.

MUNDESLEY SANATORIUM

MUNDESLEY, NORFOLK

TERMS FROM 16 GUINEAS WEEKLY (Single Room). Waiting list: 2 weeks

" " 13 " " (Shared Room). Immediate vacancies

Medical Superintendents:

E. C. WYNNE-EDWARDS, M.B.(Cantab.), F.R.C.S.(Edin.)

GEORGE H. DAY, M.D.(Cantab.)

For all information apply THE SECRETARY

Telephone: Mundesley 94 and 95 (2 lines)

CLIFFDEN, TEIGNMOUTH

For the early treatment of nervous disorders and patients needing rest and care

A well-appointed House with spacious balconies and extensive views of the South Devon Coast. Beautiful garden and own dairy in 35 acres In the same grounds, **ROWDENS**, a comfortable house with lovely views. Private road to the beach
There is also a charming house, **EBWORTHY, MANATON, DARTMOOR**, situated in 25 acres, 1100 ft. up for bracing moorland air
Resident Physicians—BERTHA M. MULES, M.D., B.S. ANNE S. MULES, M.R.C.S., L.R.C.P. *Telephones*—TEIGNMOUTH 289 and 537

CHEADLE ROYAL CHEADLE CHESHIRE

A Registered Hospital for MENTAL DISEASES and its Seaside Branch, GLAN-Y-DON, Colwyn Bay, N. Wales

The object of this Hospital is to provide the most efficient means for the treatment and care of patients of both sexes suffering from MENTAL and NERVOUS DISEASES. The Hospital is governed by a Committee appointed by Trustees. Deep and Modified Insulin Coma; E.C.T., and Psychotherapeutic treatment given. VOLUNTARY, TEMPORARY, AND CERTIFIED PATIENTS RECEIVED.

For Terms and further information apply to the MEDICAL SUPERINTENDENT *Telephone*: **GATLEY 2231**

Academic and Educational

UNIVERSITY OF LONDON
INSTITUTE OF CHILD HEALTH

DISEASE IN THE YOUNG ANIMAL AND THE CHILD

A Course of Lectures for Postgraduates will be given at The Hospital for Sick Children, Great Ormond-street, London, W.C.1, during OCTOBER-DECEMBER, 1952, on MONDAYS at 5.30 P.M.

13th Oct... Links Between Comparative Pathology and Paediatrics .. Dr. W. C. OSMAN HILL
20th Oct... Inborn Errors of Metabolism in Animal and Child .. Dr. H. HARRIS
27th Oct... Some Aspects of Deficiency Diseases of Young Animals .. Dr. J. T. ABRAMS
3rd Nov... Animal Epidemiology .. Prof. N. J. SCORGIE
10th Nov... The Pathogenesis and Control of some Diseases of Newborn Animals .. Prof. T. H. BOSWORTH
17th Nov... Aspects of Pre-natal Mortality in Domestic Animals .. Mr. S. L. HIGNETT
24th Nov... Resistance and Susceptibility to Viruses .. Prof. W. I. B. BEVERIDGE
1st Dec... Animal Genetics and Diseases in Children .. Dr. H. GRÜNEBERG
8th Dec... Virus Infections Before and After Birth .. Dr. C. H. ANDREWES
15th Dec... Comparative Physiology .. Prof. E. C. AMOROSO

The fee for the course of 10 lectures is £2 2s., for a single lecture 5s.

Applications for tickets of admission, accompanied by a remittance, should be sent to the Secretary, Institute of Child Health, The Hospital for Sick Children, Great Ormond-street, London, W.C.1. Early application is advised as the number of tickets is limited.

L.M.S.S.A.

FINAL EXAMINATION: SURGERY, 13th October, 10th November, 1st December, 1952. MEDICINE, PATHOLOGY, 20th October, 17th November, 8th December, 1952. MIDWIFERY, 21st October, 18th November, 9th December, 1952. MASTERY OF MIDWIFERY, May and November. DIPLOMA IN INDUSTRIAL HEALTH, July and December.

For regulations apply REGISTRAR, Apothecaries' Hall, Black Friars-lane, London, E.C.4.

INSTITUTE OF CHILD HEALTH
UNIVERSITY OF LONDON

Sir THOMAS FAIRBANK, D.S.O., O.B.E., M.S., F.R.C.S., will deliver the ALEX SIMPSON SMITH LECTURE for 1952, on FRIDAY, 10TH OCTOBER, 1952, at 5 P.M. at the Hospital for Sick Children, Great Ormond-street, W.C.1.

Subject: "Recent Knowledge of Affections of the Skeleton in Children."

Admission by ticket only.

Apply: the Dean, Institute of Child Health, the Hospital for Sick Children, Great Ormond-street, W.C.1.

INSTITUTE OF UROLOGY
in association with
ST. PETER'S, ST. PAUL'S, AND ST. PHILIP'S HOSPITALS

INTENSIVE COURSE IN GENITO-URINARY SURGERY FOR STUDENTS STUDYING FOR THE HIGHER EXAMINATIONS
1ST–15TH OCTOBER, 1952

The practice of the Hospitals will be open to all students attending the course. As far as possible, lecturers will illustrate their subjects with material from the outpatients, wards and museums. The use of the library and reading-room at the Institute's premises is available to all students attending the course. The fee for the course is 10 guineas payable in advance.

Applications to be made to the Secretary, Institute of Urology, 10, Henrietta-street, Covent Garden, London, W.C.2.

UNIVERSITY OF ST. ANDREWS. Eastern Regional HOSPITAL BOARD, SCOTLAND. Applications are invited for the post of LECTURER IN ORTHOPÆDICS in the Medical School, Dundee. Salary £1500 p.a., rising by £100 annually to £2000 p.a., with F.S.S.U. Benefits and Children's allowances. Grant towards removal expenses may be paid. An honorary appointment as Assistant Surgeon (with Consultant status) in the Orthopædic Department in the Dundee Royal Infirmary will be associated with the post.

Further particulars from the Secretary, The University, St. Andrews, with whom applications (1 copy), giving the names of 3 referees, should be lodged not later than 22nd October, 1952.

INSTITUTE OF ORTHOPÆDICS

COURSE IN ADVANCED CLINICAL ORTHOPÆDICS—1
6TH–11TH OCTOBER, 1952
PROVISIONAL PROGRAMME

Monday, 6th October, Town Section
10.00 A.M.–11.00 A.M. Some General Bone Diseases .. Mr. H. J. BURROWS
11.15 A.M.–12.15 P.M. Rickets .. .. .. Dr. R. NASSIM
2.00 P.M.–3.30 P.M. Clinical Demonstration .. Mr. K. I. NISSEN
Tuesday, 7th October, Country Section
10.00 A.M.–NOON Clinical Demonstration .. Mr. R. Y. PATON
2.00 P.M.–3.30 P.M. Early Tendon Transplantation in poliomyelitis .. Mr. H. J. SEDDON
Wednesday, 8th October, Town Section
10.00 A.M.–11.00 A.M. Bone Growth and Repair .. Dr. H. A. SISSONS
11.15 A.M.–12.15 P.M. Dupuytren's Contracture .. Mr. T. L. CARR
2.00 P.M.–3.00 P.M. Congenital Disorders of the Skeleton .. Mr. A. T. FRIPP
Thursday, 9th October, Town Section
9.45 A.M.–11.15 A.M. Clinical Demonstration .. Mr. V. H. ELLIS
11.30 A.M.–12.30 P.M. Recent Advances in Bacteriology .. Dr. C. H. LACK
2.00 P.M.–3.00 P.M. Topic to be chosen by those attending. Suggestions from applicants welcomed
3.00 P.M.–4.00 P.M. Prescription of Apparatus .. Mr. J. A. CHOLMELEY
Friday, 10th October, Country Section
10.00 A.M.–NOON Plastic Materials in Orthopædics .. Dr. J. T. SCALES
2.00 P.M.–4.00 P.M. Clinical Demonstration .. Mr. D. TREVOR
Saturday, 11th October, Country Section
10.00 A.M.–NOON Orthopædic Appliances .. Mr. W. TUCK

The fee for the course (including lunch and tea) is 7 guineas.

Early application should be made to the Dean at 234, Great Portland-street, London, W.1.

GUY'S HOSPITAL MEDICAL SCHOOL. Applications are invited for a Whole-time RESEARCH STUDENTSHIP at Guy's Hospital, to carry out physiological and clinical investigations into congenital heart-disease. Salary £550–£750 p.a. according to experience. Duties to commence as soon as possible after 1st October, 1952.

Applications, giving the names of 2 referees, to be sent to the Dean, Guy's Hospital Medical School, London Bridge, S.E.1, not later than 27th September, 1952.

THE LONDON HOSPITAL MEDICAL COLLEGE (UNIVERSITY OF LONDON). Applications are invited for the post of JUNIOR LECTURER IN BACTERIOLOGY. Initial salary according to age and experience on a scale £700–£100–£1100, together with membership of the F.S.S.U. and family allowances.

Applications (3 copies), giving age, and full particulars of experience, together with the names of 2 referees, should be forwarded to the Secretary of the London Hospital Medical College, Turner-street, E.1, not later than 4th October, 1952.

THE MEDICAL RESEARCH COUNCIL have a vacancy in their Radiotherapeutic Research Unit at Hammersmith Hospital for a RADIOTHERAPIST of at least Senior Registrar status to participate in work with supervoltage therapy.

Applications should be sent to the Director, Medical Research Council Radiotherapeutic Research Unit, Hammersmith Hospital, London, W.12.

MAKERERE COLLEGE. The University College of EAST AFRICA. Applications are invited for the posts of:—
(1) LECTURER IN PATHOLOGY, and
(2) FIRST ASSISTANT IN OBSTETRICS AND GYNÆCOLOGY.

Salary £1050 p.a., plus temporary cost-of-living allowance (at present £250). Child allowance £50 p.a. per child (maximum £150 p.a.). F.S.S.U. Partly furnished accommodation at rent not exceeding 10% of salary. Free passages (including family) on appointment, termination, and leave (3 months every 2 years).

Applications (6 copies), giving full particulars of qualifications, and experience, and the names of 3 referees, should be sent to the Secretary, Inter-University Council for Higher Education in the Colonies, 1, Gordon-square, London, W.C.1, from whom further particulars may be obtained. Closing date 10th October, 1952.

Hospital Services : Senior Appointments

(See Note under Appointments, p. 542 of Text.)

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ASSISTANT ANÆSTHETIST (whole-time) required at Royal Northern Hospital, Holloway, N.7 (285 Beds with all the usual special departments). Salary scale £1300–£1750. Post vacant not later than 1st April, 1953. Appointment normally made from candidates over 32 years, but applications from candidates under that age considered. Hospital may be visited by direct appointment.

Detailed applications, giving date of birth, and names of 3 referees, to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 18th October, 1952.

ST. BARTHOLOMEW'S HOSPITAL, E.C.1. Applications are invited for the post of ASSISTANT PLASTIC SURGEON (Consultant) to work 1 half-day per fortnight, possibly increasing to 1 half-day per week later.

Applications (10 copies), with the names of 3 referees, should be submitted to the undersigned by Wednesday, 8th October, 1952. C. C. CARUS-WILSON, Clerk to the Governors.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited to fill a vacancy for a Part-time CONSULTANT ANÆSTHETIST (9 notional half-days a week) at the following Groups of hospitals :—

Greenwich and Deptford, 5 notional half-days.

Sidcup and Swanley, 4 notional half-days.

Candidates must have had wide experience in anæsthetics and hold the Diploma in Anæsthetics. Applicants may visit the hospitals concerned.

Apply, stating nationality, age, sex, qualifications, and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1. The last day for acceptance of applications will be 27th September, 1952.

Provincial

BRISTOL. UNITED BRISTOL HOSPITALS. Applications are invited for the whole-time post of CONSULTANT RADIOLOGIST in the United Bristol Hospitals. The successful candidate will work as Assistant to the Director of Radiology and will be given academic status in the University of Bristol. The terms and conditions of service negotiated between the Ministry and the Profession will apply to the appointment.

Applications, stating age, particulars of education, qualifications, and experience, and giving the names of 3 referees, should be forwarded by 20th September, 1952, to—

STEPHEN C. MERIVALE, Secretary to the Board of Governors.

Bristol Royal Infirmary, Bristol, 2.

LEEDS REGIONAL HOSPITAL BOARD invites applications from Consultants or Senior Hospital Medical Officers for appointment as Locum ANÆSTHETIST for the Hull Area at the appropriate rate of salary.

Applications, stating age, qualifications, and details of present and previous appointments, together with the names of 3 referees, should be forwarded to the Secretary, Park-parade, Harrogate, as soon as possible.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the whole-time post of TUBERCULOSIS PHYSICIAN in the Blackburn and District Hospital Centre to work under the general guidance of a Consultant. Previous experience of thoracic medicine and tuberculosis essential. Salary £1300–£50–£1750. The appointment may be made in conjunction with the Local Health Authorities concerned, for whom the appointee will carry out duties in connection with prevention, care and aftercare.

Application forms may be obtained from the Senior Administrative Medical Officer to the Board at Cheetwood-road, Manchester, 8, and should be returned to be received not later than 29th September, 1952.

NEWCASTLE REGIONAL HOSPITAL BOARD. Regional CANCER SERVICE. CONSULTANT RADIOTHERAPIST (assistant), whole-time or part-time, for 9 notional half-days per week. Salary scale £1700–£2750 whole-time, pro rata part-time. The appointee will be a member of the Regional Radiotherapy Team and will be required to visit hospitals throughout the region under the Director. Further particulars may be obtained from the Director of Radiotherapy, Royal Victoria Infirmary, Newcastle upon Tyne.

Applications, together with names and addresses of referees (preferably), or testimonials to a total of 3, to be sent to the Senior Administrative Medical Officer, "Blythswood South," Osborne-road, Newcastle upon Tyne, 2, within 28 days.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time RESIDENT CONSULTANT PSYCHIATRIST AND SUPERINTENDENT required at Cell Barnes Hospital, St. Albans, Herts (733 Beds). Post vacant 1st April, 1953. Considerable experience in all aspects of mental deficiency essential, and possession of relevant higher medical qualifications desirable. A house is available in the hospital grounds, for which a rent will be charged. Candidates may visit the Hospital by direct appointment.

Detailed applications, giving names of 3 referees, to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 18th October, 1952.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. 2 ASSISTANT ANÆSTHETISTS (whole-time) required at West Middlesex Hospital, Isleworth, Middlesex (1200 Beds with all the usual special departments). Salary scale £1300–£1750. Posts vacant not later than 1st April, 1953. Appointments normally made from candidates over 32 years, but applications from candidates under that age considered. Hospital may be visited by direct appointment.

Detailed applications, giving date of birth, and names of 3 referees, to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 18th October, 1952.

NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. PÆDIATRICIAN (Consultant) required at West Middlesex Hospital, Isleworth, Middlesex (1200 Beds). To have charge of approximately 50 beds. Whole-time or maximum sessions. Hospital may be visited by direct appointment.

Detailed applications, giving date of birth, and names of 3 referees, to Secretary, North West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 18th October, 1952.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a Whole-time ASSISTANT PSYCHIATRIST, to work under Consultant Psychiatrists at Knowle Hospital, Fareham, Hants. Salary scale £1300–£50–£1750 p.a. Candidates should possess the D.P.M. and have experience of both inpatient and outpatient work in psychiatry.

Applications (5 copies), stating date of birth, qualifications, experience, and present appointment(s), and giving the names and addresses of 3 referees, should be made by letter and sent to the Secretary (S.D.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, London, W.1, to arrive not later than 30th September, 1952. Applicants may visit the Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a Whole-time CONSULTANT PHYSICIAN to the Southampton Group of hospitals. Candidates should have wide experience in general medicine and be especially interested in the treatment and rehabilitation of the chronic sick. The Consultant appointed will have charge of outpatients and inpatients in the hospitals of the Group, will be required to undertake domiciliary visits and to establish a close liaison with general practitioners and with the local Health Authority in regard to the chronic sick.

Applications (5 copies), stating date of birth, qualifications, experience, and present appointment(s), and giving the names and addresses of 3 referees, should be made by letter and sent to the Secretary (S.D.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, London, W.1, to arrive not later than 3rd October, 1952. Applicants may visit the hospitals by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a Part-time CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST (9 half-days per week) to the Salisbury Group of hospitals. Duties will be mainly at Salisbury General Hospital and residence in the Salisbury area will be a condition of the appointment.

Applications (5 copies), stating date of birth, qualifications, experience, and present appointment(s), and giving the names and addresses of 3 referees, should be made by letter and sent to the Secretary (S.D.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, London, W.1, to arrive not later than 3rd October, 1952. Applicants may visit the hospitals by local arrangement.

SHEFFIELD REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the whole-time or maximum part-time post of CONSULTANT PATHOLOGIST, with duties mainly at the Nottingham General Hospital. Candidates must have had wide experience of all branches of pathology and special experience of morbid anatomy and histology. The successful candidate, if whole-time, will be required to reside within 10 miles of the hospital referred to.

Application forms and further details may be obtained from the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10. Completed forms must be returned to the Secretary not later than 11th October, 1952.

SHEFFIELD REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners with a higher qualification in psychiatry for the whole-time post of CONSULTANT PSYCHIATRIST at the Rauceby Hospital, Sleaford, Lincs. The successful candidate will be designated Deputy Medical Superintendent and will be required to undertake child psychiatric work in the Area.

Application forms and further details may be obtained from the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10. Completed forms must be returned not later than 11th October, 1952.

SHEFFIELD REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners holding the Diploma in Anæsthetics for the post of part-time CONSULTANT ANÆSTHETIST for 8 sessions per week. Duties will include approximately 3 sessions per week at the Barnsley Hospitals and approximately 4 sessions per week at the Montagu Hospital, Mexborough.

Application forms and further details may be obtained from the Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10. Completed forms should be returned to the Secretary not later than 11th October, 1952.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the appointment of 2 ASSISTANT PSYCHIATRISTS (Senior Hospital Medical Officer scale), at Morgannwg Hospital, Bridgend. The Hospital provides all modern methods of treatment and has active outpatient clinics including a child-guidance clinic and there is a psychological department. Candidates should preferably hold the D.P.M. and have had a wide experience in psychiatry. The successful applicants will work under the direction of the Consultant Psychiatrists. Accommodation is available.

Applications (12 copies), stating date of birth, giving a summary of qualifications, experience, previous appointments with dates, and publications, with names of 3 referees, should be addressed to the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 21 days of appearance of this advertisement.

SHEFFIELD REGIONAL HOSPITAL BOARD. Required immediately, Whole-time Locum ANÆSTHETIST, for the Barnsley Hospitals and Montagu Hospital, Mexborough, for a period of 3–6 months. Remuneration 31½ guineas or 45 guineas per week, according to status.

Applications should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a CONSULTANT PSYCHIATRIST for the Mental Deficiency Institutions in the North and Mid Wales Areas. The duties will include supervision and coördination of a number of small Mental Deficiency Institutions with a total of approximately 560 Beds. Applicants should have had a wide experience in mental deficiency and hold a Diploma in Psychological Medicine. The successful candidate will be required to reside within the Area served.

Applications (12 copies), stating date of birth, giving a summary of qualifications, experience, previous appointments with dates, and publications, with names of 3 referees, should be addressed to the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, from whom further particulars may be obtained, within 21 days of appearance of this advertisement.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a Whole-time ASSISTANT CHEST PHYSICIAN (Senior Hospital Medical Officer scale) to serve the Rhymney and Sirhowy Valleys Hospital Management Committee. The successful candidate will be based at Pontllanfraith Chest Clinic and will work under the direction of the Consultant Chest Physician. Candidates should have had wide experience in chest diseases and tuberculosis in particular.

Applications (14 copies), stating date of birth, giving a summary of qualifications, experience, previous appointments with dates, and publications, together with the names of 3 referees, should be addressed to the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 21 days of appearance of this advertisement.

Hospital Services : Junior Appointments

(See Note under Appointments, p. 542 of Text.)

BRITISH HOSPITAL FOR MOTHERS AND BABIES, Samuel-street, Woolwich, S.E.18. OBSTETRICAL HOUSE OFFICER (recognised for M.R.C.O.G.), vacant 1st November. Salary £400 or £450 p.a., less £100 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. Locum HOUSE SURGEON (resident).

Apply Hospital Secretary (Telephone : BATtersea 2445).

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in General Medical Department, including hæmatology and endocrinology. Appointment for 6 months from 1st November.

Applications, with copies of testimonials or names of 2 referees, to Medical Director by 20th September.

CENTRAL MIDDLESEX HOSPITAL, Park Royal, N.W.10. RESIDENT HOUSE OFFICER required in General Medical Department, including neurology. Appointment for 6 months from 1st November.

Applications, with copies of testimonials or names of 2 referees, to Medical Director by 20th September.

ELIZABETH GARRETT ANDERSON HOSPITAL, Euston-road, N.W.1. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from registered Women medical practitioners for the post of SECOND HOUSE PHYSICIAN to become vacant 1st October, 1952. Appointment for 6 months. Salary according to Ministry of Health scale for House Officers.

Applications, with copies of 3 recent testimonials, should be sent to the Secretary, Elizabeth Garrett Anderson Hospital, by 22nd September.

EAST END MATERNITY HOSPITAL, 384/398, Commercial-road, London, E.1. (60 Beds.) Post recognised for M.R.C.O.G. RESIDENT OBSTETRICAL OFFICER required. 6 months House Officer III—6 months Senior House Officer. National scale salaries, deduction for emoluments £100 and £156 respectively.

Applications to Secretary, Stepney Group Hospital Management Committee, Raine-street, E.1.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of SENIOR HOUSE OFFICER to the Cardiac Department. The appointment will be for 6 months in the first instance at a salary of £670 p.a.

Applications (6 copies), giving full particulars, should be addressed to the House Governor to arrive not later than 4th October, 1952. H. BRIERLEY, House Governor.

MILE END HOSPITAL, Bancroft-road, E.1. (475 Beds.) HOUSE PHYSICIAN (first, second, or third) required for 6 months to commence duty 18th October, 1952.

Application forms, to be returned by 24th September, with copies of not more than 3 testimonials, may be obtained from Physician-Superintendent.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, London, W.12. 2 HOUSE SURGEONS (radiotherapy) required. Posts vacant 15th October and 1st December.

Applications, stating age, qualifications, experience, and copies of 2 recent testimonials, to Secretary, Board of Governors, by 22nd September.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, London, W.12. PÆDIATRIC REGISTRAR (resident) required 1st November. Duties involve care of newborn babies in Maternity Department and Premature Baby Unit.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, by 22nd September.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, London, W.12.

HOUSE SURGEON (general surgery).

HOUSE SURGEON (orthopædics).

Required 1st November.

Applications, stating age, qualifications, experience, and copies of 2 recent testimonials, to Secretary, Board of Governors, by 20th September.

HAMMERSMITH HOSPITAL AND INSTITUTE OF OBSTETRICS AND CHILD HEALTH, London, W.12. Applications invited for following posts :—

HOUSE SURGEON (obstetrics), vacant 1st November.

HOUSE SURGEON (obstetrics), vacant 1st December.

Applications, stating age, qualifications, experience, copies of 2 recent testimonials, to Secretary, Board of Governors, by 22nd September.

HOSPITAL OF ST. JOHN AND ST. ELIZABETH, 60, Grove End-road, N.W.8. Applications are invited from registered medical practitioners (Male) for the appointment of HOUSE PHYSICIAN, to become vacant on Monday, 13th October, 1952. Appointment will be for a period of 6 months. Salary is at the rate of £350 p.a.

Applications should reach the Secretary on or before Saturday, 27th September, 1952, together with copies of 3 recent testimonials.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, London, E.15. Applications are invited from registered medical practitioners (Male or Female) for the appointment of JUNIOR CASUALTY OFFICER (House Officer, first, second, or third post) for 6 months commencing on 4th October, 1952.

Applications, stating age, and experience, together with copies of testimonials, should be sent to the undersigned not later than 20th September, 1952.

M. J. HUNTLEY, Group Secretary,
West Ham Group Hospital Management Committee.
Stratford, London, E.15.

QUEEN MARY'S HOSPITAL FOR THE EAST END, Stratford, London, E.15. Applications are invited from registered medical practitioners (Male) for the appointment of CASUALTY OFFICER AND DEPUTY RESIDENT SURGICAL OFFICER (Senior House Officer grade) for a period of 1 year commencing on 1st October, 1952.

Candidates should send applications, together with copies of recent testimonials, to the Group Secretary, West Ham Group Hospital Management Committee, Stratford, London, E.15, by 18th September, 1952.

ROYAL NATIONAL THROAT, NOSE AND EAR HOSPITAL, Gray's Inn-road, London, W.C.1, and Golden-square, W.1. RESIDENT HOUSE SURGEON. There will be a vacancy (second or subsequent post) on 1st October, 1952. Appointment for 6 months with salary as laid down for House Officer grades in the terms and conditions of service under the National Health Service.

Applications, stating age, qualifications, full details of previous experience (particularly in this specialty), with copies of 1–3 recent testimonials, should be sent to the undersigned immediately. JOHN H. YOUNG, House Governor and Secretary.

ROYAL NORTHERN HOSPITAL, Holloway, London, N.7. ORTHOPÆDIC HOUSE SURGEON required 2nd October, 1952. Occasional casualty duties involved. Salary £400–£450 p.a., less £100 board-residence.

Applications, stating age, nationality, qualifications, and experience, with copies of 3 testimonials, to be sent to the Hospital Secretary as soon as possible.

ROYAL FREE HOSPITAL GROUP. Applications are invited for the post of SENIOR REGISTRAR to the Department of Rheumatism of the Royal Free Hospital. The vacancy is only open to registered medical practitioners who have already completed 4 years as Senior Registrar in Medicine, and applicants should be members of the Royal College of Physicians or hold equivalent qualifications. The appointment is full-time, non-resident, and for 1 year in the first instance, but the successful candidate would be eligible for reappointment for a further period of up to 2 years. Duties are to commence on 1st November, 1952. Salary and conditions of service in accordance with those laid down by the Ministry of Health.

Application forms may be obtained from the Secretary to the Board of Governors, The Royal Free Hospital, Gray's Inn-road, London, W.C.1, to whom they should be returned not later than 7th October, 1952.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited from registered Female medical practitioners for the appointments of GYNÆCOLOGICAL HOUSE SURGEONS (2) to become vacant on 20th November, 1952, and 1st December, 1952. Posts recognised for the M.R.C.O.G. Appointments are for a period of 6 months.

For form of application apply to the Secretary at the Hospital.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited from registered Female medical practitioners for the appointment of OBSTETRIC HOUSE SURGEON to become vacant on 21st November, 1952. Post recognised for the M.R.C.O.G. Appointment is for a period of 6 months.

For form of application apply to the Secretary at the Hospital.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. Applications are invited from registered Female medical practitioners for the appointment of RESIDENT MEDICAL OFFICER at the Hospital's 50-bed country branch near Crawley, Sussex. The post, which is full-time (resident) or part-time (non-resident), is vacant from 1st November, 1952. The appointment is of Senior House Officer grade and is for 1 year.

For form of application apply to the Secretary at the Hospital.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered Women medical practitioners for the post of Part-time REGISTRAR for 2 sessions per week in the E.N.T. Department. The appointment is normally for 2 years but is subject to review annually. Canvassing will disqualify but candidates are not precluded from visiting the Hospital.

For forms of application apply (enclosing a stamped addressed envelope) to the Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to whom completed applications should be returned not later than 27th September, 1952.

SOUTH LONDON HOSPITAL FOR WOMEN AND CHILDREN, Clapham Common, S.W.4. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited from registered Women medical practitioners for the post of ANÆSTHETIC REGISTRAR (either resident or prepared to live within 20 minutes of the Hospital). D.A. desirable but not essential. Post recognised for D.A. The appointment is normally for 2 years, but is subject to review annually. Canvassing will disqualify but candidates are not precluded from visiting the Hospital if they so desire.

For forms of application apply (enclosing a stamped addressed envelope) to the Secretary, Lambeth Group Hospital Management Committee, Renfrew-road, S.E.11, to whom completed applications should be returned not later than 27th September, 1952.

SOUTH EAST REGIONAL THORACIC SURGERY UNIT. (40 Beds.) BROOK GENERAL HOSPITAL, Shooters Hill-road, S.E.18. SENIOR HOUSE OFFICER (recognised for F.R.C.S.), vacant 28th October. The Unit treats all types of chest diseases and offers opportunity for comprehensive training in thoracic surgery. Appointment for 6 months in first instance and may be renewed for further period. Salary £670, less £150 p.a. for residence.

Apply to Group Secretary, Memorial Hospital, Woolwich, S.E.18.

SOUTH EAST METROPOLITAN REGIONAL HOS-PITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Anæsthetics to fill a vacancy in the approved trainee establishment at the Greenwich and Deptford Group of hospitals. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staff (England and Wales) and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications, and experience, with relevant dates, together with the names and addresses of 3 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 27th September, 1952.

ST. ANN'S GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON (third post) to the above Hospital for a period of 6 months. Post vacant 1st October, 1952.

Application form from the Secretary, Tottenham Group Hospital Management Committee, The Green, N.15.

ST. MARY'S HOSPITAL FOR WOMEN AND CHILDREN, Upper-road, Plaistow, London, E.13. Applications are invited for the combined appointment of RESIDENT CASUALTY OFFICER/DEPUTY RESIDENT SURGICAL OFFICER (Senior House Officer grade) for a period of 1 year, commencing as soon as possible.

Candidates should send applications, together with copies of recent testimonials, to the Group Secretary, West Ham Group Hospital Management Committee, Stratford, London, E.15, by 20th September, 1952.

ST. GEORGE'S HOSPITAL, S.W.1. Applications are invited for the post of RESIDENT MEDICAL OFFICER in the grade of Senior House Officer at St. George's Hospital, Hyde Park Corner. The appointment is for 1 year from 1st November, 1952, and the successful candidate should be prepared to take up duty on 17th October, 1952.

Applications, together with the names of 2 referees, should reach the undersigned not later than 25th September, 1952.

P. H. CONSTABLE, House Governor.

ST. GEORGE-IN-THE-EAST HOSPITAL, Raine-street, Wapping, E.1. Applications are invited for the post of HOUSE PHYSICIAN (House Officer, first, second, or third). Salary, &c., in accordance with national scale. Tenable for 6 months. Post vacant on 8th October, 1952.

Applications to the Medical Superintendent. Closing date 29th September, 1952.

ST. JAMES' HOSPITAL, Ouseley-road, Balham, S.W.12 Applications are invited immediately for the post of SENIOR HOUSE OFFICER (anæsthetics).

Applications should state age, qualifications, experience, and the names of 2 referees, and should be sent to the Group Secretary, Wandsworth Hospital Group, 14, Atkins-road, Balham, S.W.12, immediately.

ST. STEPHEN'S HOSPITAL, Fulham-road, Chelsea, S.W.10. HOUSE PHYSICIAN to Pædiatric Department, vacancy 1st October, 1952.

Applications, naming 2 referees, to the Medical Superintendent as soon as possible.

WANSTEAD HOSPITAL, Wanstead, E.11. (191 Beds.) Applications are invited for the post of CASUALTY OFFICER (graded as Senior House Officer), vacant 29th September, 1952. Recognised for F.R.C.S. Salary £670 p.a., with a deduction of £120 p.a. for board, lodging, &c.

Applications, giving full particulars, together with copies of 2 recent testimonials, should be sent immediately to the Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be a vacancy on 15th December, 1952, for a HOUSE PHYSICIAN (Senior House Officer).

Further particulars and form of application which must be returned not later than 6th October, 1952, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

UNIVERSITY COLLEGE HOSPITAL, Gower-street, W.C.1. Applications are invited for the post of REGISTRAR (£775–£890 p.a.) to the X-ray Diagnostic Department to start on 1st October, 1952, or as soon as possible thereafter.

Applications, with the names of 2 referees, to the Administrator and Secretary by 20th September.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications are invited for the post of SURGICAL REGISTRAR for 1 year in the first instance, commencing 24th November, 1952. The appointment is subject to the terms and conditions of service for hospital medical and dental staffs.

Applications (6 copies), with the names of 2 referees, should reach the House Governor by 20th September, 1952.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications are invited for the post of MEDICAL SENIOR REGISTRAR. The appointment is for 1 year in the first instance and the successful candidate will be expected to take up his duties as soon as possible. Candidates must be Members of the Royal College of Physicians.

Applications (10 copies), with the names of 3 referees, should be sent to CHARLES M. POWER, House Governor and Secretary, by 27th September, 1952.

WESTMINSTER HOSPITAL, St. John's-gardens, S.W.1. Applications are invited for the post of REGISTRAR to the Department of Anæsthetics for 1 year in the first instance as from 1st November, 1952.

Applications (10 copies), with the names of 2 referees, should be sent to CHARLES M. POWER, House Governor and Secretary, by 27th September, 1952.

WEST LONDON HOSPITAL, Hammersmith-road, W.6. RESIDENT HOUSE OFFICER (anæsthetics) required immediately.

Applications, stating age, qualifications, experience, copies of 2 testimonials, to Secretary by 22nd September.

WEST LONDON HOSPITAL, Hammersmith-road, W.6. Full-time NON-RESIDENT REGISTRAR (chemical pathology) required immediately.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, Hammersmith, West London, and St. Mark's Hospitals, London, W.12, by 27th September.

Provincial

AYRSHIRE. KILMARNOCK INFIRMARY. (147 Beds.) Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER (surgical) due to become vacant on 13th October.

Applications, together with copies of 2 testimonials, to the Area Medical Superintendent, 1, Hill-street, Kilmarnock, immediately.

AYRSHIRE. BALLOCHMYLE HOSPITAL, Mauchline. (388 Beds.) Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER (medical), now vacant. Appointment tenable for 1 year, and offers a wide variety of experience. Salary £670, less £150 for full residential emoluments.

Applications, together with copies of 2 testimonials, to Area Medical Superintendent, Ballochmyle Hospital, immediately.

APPLEY BRIDGE, near WIGAN. WRIGHTINGTON HOSPITAL. SENIOR HOUSE OFFICER required. Manchester Regional Centre for orthopædic tuberculosis. 200 adults and 100 children. £670 less board.

Apply to Consultant Surgeon-Superintendent with references.

ASHTON, HYDE, AND GLOSSOP HOSPITAL MANAGE-MENT COMMITTEE. Applications are invited from registered medical practitioners for the following appointments :—

Ashton-under-Lyne General Hospital (800 Beds)

E.N.T. SURGEON (Senior House Officer grade) required, mainly for duty at District Infirmary, Ashton-under-Lyne (200 Beds). Post recognised for F.R.C.S. (Eng.).

HOUSE PHYSICIAN, with duties at other hospitals, vacant now.

HOUSE SURGEON (general surgery), vacant now. Post recognised for F.R.C.S. (Eng.).

Appointments are subject to Ministry of Health terms and conditions of service.

Applications, giving age, nationality, qualifications, and experience, with copies of 3 testimonials, should be forwarded to R. W. MCVITY, Group Secretary.

Astley-road, Stalybridge, Cheshire.

ABERDEEN ROYAL INFIRMARY. Board of Management FOR THE ABERDEEN GENERAL HOSPITALS. Applications are invited for the appointment of a SENIOR HOUSE OFFICER for the Neurosurgical Unit at the above Hospital for a period of duty to 31st March, 1953. The appointment, which is resident, is subject to the conditions of service issued by the Department of Health for Scotland.

Applications, with full details, should be lodged immediately with the Secretary, Aberdeen General Hospitals, 62, Queen's-road, Aberdeen.

ABERDEEN ROYAL INFIRMARY. Board of Management FOR THE ABERDEEN GENERAL HOSPITALS. HOUSE OFFICER in Ophthalmology required at the above Hospital to commence duty immediately. The appointment which is resident, is subject to the conditions of service issued by the Department of Health for Scotland.

Applications, with full details, should be lodged, as soon as possible, with the Secretary, Aberdeen General Hospitals, 62, Queen's-road, Aberdeen.

ABERDEEN GENERAL HOSPITALS BOARD OF MANAGEMENT. ABERDEEN ROYAL INFIRMARY. WOODEND GENERAL HOSPITAL. Applications are invited for the following posts in Anæsthetics at the above Hospitals :—

(1) JUNIOR HOSPITAL MEDICAL OFFICER in Anæsthetics.

(2) SENIOR HOUSE OFFICER in Anæsthetics. This appointment will be for a period of 1 year, and applicants should have had previous experience in general medicine and surgery.

Both appointments are subject to the conditions of service issued by the Department of Health for Scotland.

Applications, giving details of qualifications, and experience, with the names of 2 referees, should be lodged with the Secretary, Aberdeen General Hospitals, 62, Queen's-road, Aberdeen, within 14 days of the appearance of this advertisement.

AMERSHAM GENERAL HOSPITAL, Bucks. Resident HOUSE SURGEON required 28th September.

Apply Secretary.

ASHFORD HOSPITAL, Ashford, Middlesex. Staines GROUP HOSPITAL MANAGEMENT COMMITTEE. Required, RESIDENT SENIOR HOUSE OFFICER (Male) for general medical duties. National Health Service salary scale and conditions of service. Post vacant mid-October.

Applications, stating age, qualifications, and experience, with copies of up to 3 recent testimonials, to Medical Director of Hospital by 27th September, 1952.

AYLESBURY. ROYAL BUCKINGHAMSHIRE HOS-PITAL. HOUSE SURGEON for Department of Ophthalmology which is centred on this Hospital, and which conducts work at peripheral clinics. Vacant end of September. Post is recognised for D.O., and duties will include some children's surgery.

Applications, together with 2 testimonials, to Secretary-Superintendent, as soon as possible.

AYLESBURY. ROYAL BUCKINGHAMSHIRE HOS-PITAL. HOUSE SURGEON for Accident and Orthopædic Department, which is centred on this Hospital and comprises 40 beds. First or second post, vacant end of September.

Applications, together with 2 testimonials, to Secretary-Superintendent as soon as possible.

AYLESBURY. STOKE MANDEVILLE HOSPITAL. JUNIOR HOSPITAL MEDICAL OFFICER required for Spinal Injuries Centre. Salary £700–£50–£1000 p.a.

Applications, with 2 testimonials, to the Administrative Officer as soon as possible.

AYLESBURY. STOKE MANDEVILLE HOSPITAL. (624 Beds.) HOUSE PHYSICIAN for Pædiatric Department. Post qualifies for D.C.H. and duties will include care of children in Infectious Diseases Unit, Plastic Unit, and Outpatient's Department, Royal Buckinghamshire Hospital.

Applications, giving full details of age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, should be sent to the Administrative Officer, Stoke Mandeville Hospital, Aylesbury.

AYLESBURY. STOKE MANDEVILLE HOSPITAL. (624 Beds.) 2 HOUSE PHYSICIANS. The medical beds are situated at this Hospital but candidates appointed will also be required to attend the Royal Buckinghamshire Hospital Outpatient's Department.

Applications, giving full details of age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, should be sent immediately to the Administrative Officer, Stoke Mandeville Hospital, Aylesbury.

BARROW-IN-FURNESS. NORTH LONSDALE HOS-PITAL. BARROW AND FURNESS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for a post of RESIDENT SENIOR HOUSE OFFICER (surgical) at the above Hospital (189 Beds), with surgical work under control of Consultant Surgeons. This post is recognised for the F.R.C.S. examinations. Salary £670 p.a., less £155 p.a. for residential emoluments.

Applications, stating age, qualifications, and experience, with copy testimonials or names of referees, to be forwarded to the Group Secretary, 52, Paradise-street, Barrow-in-Furness.

BARROW-IN-FURNESS. NORTH LONSDALE HOS-PITAL. BARROW AND FURNESS HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for a post of RESIDENT HOUSE SURGEON at the above Hospital (189 Beds), with surgical work under control of Consultant Surgeons. This post is recognised for the F.R.C.S. examinations. National conditions and salary scale (House Officer grade).

Applications, stating age, qualifications, and experience, with copy testimonials or names of referees, to be forwarded to the Group Secretary, 52, Paradise-street, Barrow-in-Furness.

BARNET. CLARE HALL HOSPITAL, South Mimms, BARNET, HERTS. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR (Resident Surgical Officer) required for the Thoracic Unit at above Hospital, which has 504 Beds, including 76 for tuberculous and non-tuberculous thoracic surgery. Candidates may visit Hospital by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, Barnet Group Hospital Management Committee, 1, Wellhouse-lane, Barnet, Herts, by 23rd September, 1952.

BARNET GENERAL HOSPITAL, Barnet, Herts. CASUALTY OFFICER (Senior House Officer grade) required, 1 year commencing 13th October.

Applications, giving age, nationality, qualifications, and experience, with copies of 3 testimonials, to be sent to the Hospital Secretary.

BANBURY, OXON. HORTON GENERAL HOSPITAL. (170 Beds.) HOUSE SURGEON required immediately for general surgical and gynæcological beds. 4 other residents. Post tenable 6 months in first instance. Salary from £350, according to experience. Hospital recognised for 6 months training F.R.C.S. (Eng.).

Applications, stating age, nationality, qualifications, and names of 2 referees, to the Secretary.

BANBURY, OXON. HORTON GENERAL HOSPITAL CASUALTY OFFICER AND ORTHOPÆDIC HOUSE SURGEON (Senior House Officer grade) required. Acute Hospital with 170 Beds ; active Surgical Department with considerable emergency work. 4 other residents.

Applications, stating age, nationality, qualifications, and names of 2 referees, to the Secretary.

BANBURY, OXON. HORTON GENERAL HOSPITAL. (170 Beds.) SENIOR HOUSE OFFICER (Surgeon) required on or before 1st October. 4 other residents. Active Surgical Department under direction of resident Consultant. Recognised 6 months training F.R.C.S. (Eng.).

Applications, stating age, nationality, qualifications, and names of 2 referees, to the Secretary.

BARNSLEY. BECKETT HOSPITAL. Sheffield Regional HOSPITAL BOARD. Applications are invited from registered medical practitioners for the whole-time post of REGISTRAR (anæsthetics) to the above Hospital. The appointment is for 1 year in the first instance and may be renewed for a further year.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10, to arrive not later than 22nd September, 1952.

BATLEY. THE GENERAL HOSPITAL. Carlinghow HILL, BATLEY, YORKS. (99 Beds.) Applications are invited for the appointments of :—

HOUSE SURGEON (E.N.T. and orthopædic).

HOUSE SURGEON (ophthalmic and general surgery).

This General Hospital provides all the inpatient treatment for the Group in the specialties of orthopædics, E.N.T., and ophthalmology in addition to some general surgery, together with the usual outpatient clinics.

Applications, stating age, qualifications, and experience, together with recent testimonials should be submitted immediately to the Administrative Officer.

BEDFORD GROUP HOSPITAL MANAGEMENT COM-MITTEE. Locum REGISTRAR required for busy acute Orthopædic and Traumatic Department on 15th September, 1952.

Applications, stating age, nationality, qualifications, and previous appointments, together with copies of 2 recent testimonials, should be forwarded to the Group Secretary, 3, Kimbolton-road, Bedford.

BEVERLEY, YORKS. WESTWOOD HOSPITAL. Senior ORTHOPÆDIC HOUSE SURGEON required immediately. The post is recognised for the F.R.C.S. Salary £670, less a charge of £140 for board and lodging.

Applications to the Secretary.

BISHOP'S STORTFORD, HERTS. HAYMEADS HOS-PITAL. (350 occupied beds. Midway between London and Cambridge. Main Line Railway from Liverpool Street.) Applications are invited from registered medical practitioners for the following resident appointment of SENIOR HOUSE OFFICER (pathology). Salary £670 p.a., less £130 p.a. in respect of residential emoluments. The appointment is for a period of 1 year, duties to commence 1st October, 1952.

Applications, giving fullest details, together with copies of recent testimonials or the names of referees, to the Administrative Officer.

BISHOP'S STORTFORD, HERTS. HAYMEADS HOS-PITAL. (350 occupied beds. Midway between London and Cambridge. Main Line Railway from Liverpool Street.) Applications are invited from registered medical practitioners for the appointment of a Whole-time Temporary REGISTRAR (anæsthetics) at the above Hospital. Appointment to commence immediately, for approximately 6-month period. Salary at the rate of £775–£890 p.a., less £130 p.a. for residential emoluments.

Applications, giving fullest details, together with copies of recent testimonials or the names of referees, to the Administrative Officer.

BISHOP'S STORTFORD, HERTFORDSHIRE. HAY-MEADS HOSPITAL. (350 occupied beds. Midway between London and Cambridge. Main Line railway from Liverpool Street.) Applications are invited from registered medical practitioners for the following :—

HOUSE OFFICER (medical), Male or Female, first, second, or third post held, with primary attachment to the pædiatric ward of 24 beds, and other duties in connection with 8 skin beds and the Casualty Department. Salary £350–£450 p.a.

HOUSE OFFICER (medical), Male or Female, first or second post held. Salary £350–£400 p.a.

Both appointments to commence 1st October, 1952, for a period of 6 months, and subject to deduction for residential emoluments of £100 p.a.

Applications, stating nationality, age, qualifications, and experience, with copies of recent testimonials or the names of referees, should be sent to the Administrative Officer as soon as possible.

BISHOP AUCKLAND. THE GENERAL HOSPITAL. Applications are invited for the post of Locum Tenens HOUSE SURGEON/CASUALTY OFFICER (Senior House Officer), with duties in orthopædic and general surgical wards, and offering opportunity for minor and traumatic surgery. Salary £670 p.a., less deductions for residential emoluments.

Applications, giving age, qualifications, and experience, together with 3 testimonials to be sent to the undersigned as soon as possible.

K. G. T. LUXFORD, Secretary/Finance Officer,
South West Durham Hospital Management Committee.

BIRMINGHAM. ROYAL ORTHOPÆDIC HOSPITAL, Broad-street, BIRMINGHAM, 15. (Acute Orthopædic Hospital with 338 Beds and extensive outpatient service.) Applications are invited from registered medical practitioners, preferably with previous orthopædic experience, for SENIOR HOUSE OFFICER.

Applications, with copies of testimonials, to the Administrator.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Applications invited for the following whole-time appointments :—

(*a*) SURGICAL REGISTRAR (Resident Surgical Officer), Coventry Group. Successful candidate will act as Resident Surgical Officer to Manor Hospital, Nuneaton (139 Beds) and George Eliot Hospital, Nuneaton (258 Beds). Experience in specialty essential.

(*b*) REGISTRAR in General Surgery, Wolverhampton Group. Duties at Royal Hospital, Wolverhampton (310 Beds), recognised for F.R.C.S. Successful candidate must be resident. Experience in specialty essential.

(*c*) REGISTRAR in Dermatology, Wolverhampton Group. Duties mainly at Royal Hospital, Wolverhampton (310 Beds). Non-resident appointment. Experience in specialty essential and possession of higher qualification an advantage.

(*d*) REGISTRAR in Pathology, Coventry Group. Duties at Group Laboratory at Coventry and Warwickshire Hospital. Applicants must have some experience in pathology, and an interest in hæmatology is desirable.

(*e*) REGISTRAR in Physical Medicine, Coventry Group. Duties mainly at Coventry and Warwickshire Hospital (346 Beds) and Manor Hospital, Nuneaton (139 Beds). Non-resident appointment.

(*f*) REGISTRAR in Anæsthetics, Birmingham (Dudley Road) Group. Duties mainly at Dudley Road Hospital (800 Beds) and Birmingham Eye Hospital (156 Beds), and at other hospitals in the group as required. Resident or non-resident appointment. Experience in specialty desirable.

(*g*) REGISTRAR in Pathology, West Bromwich Group. Duties mainly at Hallam Hospital, West Bromwich (440 Beds). Non-resident appointment.

Application forms from Secretary, 10, Augustus-road, Birmingham, 15, to be returned before 29th September, 1952.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Applications invited for appointment of Whole-time Locum Tenens ORTHOPÆDIC REGISTRAR, South Warwickshire Group. Duties mainly at Warwick Hospital, Warwick (350 Beds including 52 orthopædic). Non-resident appointment. Experience in specialty desirable. Appointment for a period of 2–3 months commencing 1st October, 1952.

Applications (4 copies), stating name, age, nationality, qualifications, present and previous appointments, and details of 3 referees to Secretary, 10 Augustus-road, Birmingham, 15, immediately.

BIRMINGHAM REGIONAL HOSPITAL BOARD. Applications invited for appointment of Whole-time SENIOR REGISTRAR in General Surgery, Stoke-on-Trent Group. Duties mainly at City General Hospital, Stoke (956 Beds). Resident or non-resident appointment. Higher qualification required. Experience in specialty essential. The successful candidate may subsequently be required to spend not more than 2 years in a selected hospital of the United Birmingham Hospitals in accordance with the arrangements for the interchange of registrars agreed between the 2 Boards.

Application forms from Secretary, 10, Augustus-road, Birmingham, 15, to be returned before 29th September, 1952.

BIRMINGHAM ACCIDENT HOSPITAL, Bath-row, BIRMINGHAM, 15. (215 Beds.) Applications are invited for the following appointments :—

RESIDENT SURGICAL OFFICER (Senior House Officer grade), vacant 1st October, 1952. The salary will be at the rate of £670 p.a., and a deduction of £140 p.a. will be made in respect of emoluments.

HOUSE SURGEONS (2 now vacant), Male or Female. The appointments will be for a period of 6 months, of which 2 may be spent in the Burns Unit (Medical Research Council). Recognised for F.R.C.S.

The Hospital is the largest Traumatic Unit in the country, and treats 50,000 new patients each year. The posts offer ample opportunity for practical experience in the management of all types of injury and teaching by the Consultant Staff.

Applications, accompanied by copies of recent testimonials or names of 2 referees, to the Administrator.

BIRMINGHAM, 29. SELLY OAK HOSPITAL. Applications are invited for the appointment of SENIOR HOUSE OFFICER (pædiatrics). Recognised for D.C.H. Salary £670 p.a., post tenable in the first instance for 6 months. Vacancy in October.

Applications, stating qualifications, experience, and age, to the Medical Superintendent, with copies of 3 testimonials.

BIRMINGHAM AND MIDLAND EYE HOSPITAL, Church-street, BIRMINGHAM, 3. Required, HOUSE SURGEON to take up duty immediately. Appointment will be for 6 months but renewable, and will enable successful candidate to prepare for the Diploma in Ophthalmology.

Applications, stating age, nationality, qualifications, and experience, to Secretary, Management Committee, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. QUEEN ELIZABETH HOSPITAL. Applications are invited for the post of MEDICAL REGISTRAR (non-resident, registrar grade) now vacant in the Medical Professorial Unit, tenable for 1 year in the first instance. Candidates must be registered medical practitioners, have held a resident appointment in a teaching hospital, and should possess the M.R.C.P. Opportunity will be given to the successful candidate to take part in cardio-respiratory research.

Forms of application may be obtained from, and should be returned not later than 15th October to, the Secretary, United Birmingham Hospitals, Queen Elizabeth Hospital, Birmingham, 15.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. HOUSE OFFICER (casualty) required to commence duty on 1st October, 1952, for 6 months.

Forms of application may be obtained from the House Governor, and should be returned not later than 26th September, 1952. G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. HOUSE OFFICER (surgical) required for 6 months, to commence duty on 1st November, 1952. The duties will be mainly general surgery, but the Officer will have, in addition, the opportunity of undertaking a certain amount of special surgery.

Forms of application may be obtained from the House Governor, and should be returned not later than 27th September, 1952. G. A. PHALP, Secretary to the Board of Governors.

BLACKPOOL. VICTORIA HOSPITAL. (339 Beds.)

(1) SENIOR HOUSE OFFICER (E.N.T. Department). Post recognised for D.L.O. and F.R.C.S.

(2) 2 RESIDENT HOUSE SURGEONS (Surgical Department). Posts recognised for F.R.C.S.

(3) HOUSE OFFICER (Casualty and Orthopædic Department). Post recognised for F.R.C.S.

National Health Service salary and conditions of service.

Applications, with references, should be sent to the Hospital Secretary, Victoria Hospital, Blackpool.

BRADFORD CHILDREN'S HOSPITAL. (102 Beds.) HOUSE OFFICER (Female), vacant 10th October. Salary £350–£450 p.a., less £100 p.a. residential emoluments. Hospital recognised for D.C.H.

Applications, stating age, nationality, qualifications, and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRADFORD. ROYAL EYE AND EAR HOSPITAL.

HOUSE SURGEON (E.N.T.), vacant now.

HOUSE SURGEON (ophthalmic), vacant 1st October.

Hospital recognised for F.R.C.S., D.L.O., and D.O.M.S. Salary for above posts £350–£450 p.a., less £100 p.a. residential emoluments.

Applications, stating age, nationality, qualifications, and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRADFORD. ROYAL EYE AND EAR HOSPITAL. SENIOR HOUSE SURGEON (E.N.T.), vacant now. Hospital recognised for D.L.O. and F.R.C.S. Salary £670 p.a., less £130 p.a. residential emoluments.

Applications, stating age, nationality, qualifications and experience, with copy testimonials, to Secretary, Bradford Royal Infirmary.

BRADFORD ROYAL INFIRMARY.

HOUSE SURGEON (general and urology), vacant 1st October.

HOUSE SURGEON (Thoracic Unit), vacant now.

Salary for above posts £350–£450 p.a., less £100 p.a. residential emoluments.

Applications, stating age, nationality, qualifications, and experience, with copy testimonials to Secretary.

BRADFORD ROYAL INFIRMARY. House Physician, vacant 1st November. Salary £350–£450 p.a., less £100 p.a. residential emoluments.

Applications, stating age, nationality, qualifications, and experience, with copy testimonials, to Secretary.

BRADFORD. ST. LUKE'S HOSPITAL.

SENIOR ORTHOPÆDIC HOUSE SURGEON/CASUALTY OFFICER, vacant now. Recognised for F.R.C.S.

SENIOR HOUSE SURGEON (general), vacant now. Recognised for F.R.C.S.

Salary for above 2 posts £670 p.a., less £130 p.a. residential emoluments.

ORTHOPÆDIC HOUSE SURGEON/CASUALTY OFFICER, vacant 1st October. Recognised for F.R.C.S. Salary £350–£450 p.a., less £100 p.a. residential emoluments.

Applications for all above posts, stating age, nationality, qualifications, and experience, with copy testimonials to Secretary, Bradford Royal Infirmary.

BURTON-ON-TRENT GENERAL INFIRMARY. (Acute General Hospital—235 Beds.) Applications are invited to fill the following vacancies :—

(*a*) RESIDENT HOUSE SURGEON to General Surgical and Gynecological Units.

(*b*) RESIDENT HOUSE SURGEON for General Surgical duties.

The posts offer excellent experience.

Applications, with all details, and copies of recent testimonials, should be addressed to—

J. E. SMITH, Group Secretary,
Burton-on-Trent Hospital Management Committee.

BURY AND ROSSENDALE HOSPITAL MANAGEMENT COMMITTEE.

Bury General Hospital

SENIOR HOUSE OFFICER (orthopædics).

HOUSE SURGEON. This post is recognised for the F.R.C.S.

SENIOR HOUSE OFFICER (medical), 40 acute beds.

SENIOR HOUSE OFFICER (surgical).

Rossendale General Hospital

HOUSE SURGEON.

Fairfield General Hospital

JUNIOR HOSPITAL MEDICAL OFFICER. Mainly for psychiatric duties.

Applications are invited for the above posts and should indicate age, nationality, qualifications, and experience, and should be sent to the undersigned as soon as possible.

H. WILKINSON, Secretary to the Committee.

Bury General Hospital, Bury, Lancs.

BRISTOL. COSSHAM/FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. FRENCHAY HOSPITAL. HOUSE SURGEON (Thoracic Surgery Department). Vacancies occur shortly in the above department, which is the Regional Thoracic Surgery Centre (120 Beds) for the South West.

Applications, with full particulars, should be addressed to the Group Secretary, Frenchay Hospital, Bristol, quoting "Thoracic."

BRISTOL (near). HORTHAM-BRENTRY HOSPITAL GROUP MANAGEMENT COMMITTEE. JUNIOR HOSPITAL MEDICAL OFFICER (Male, age-limit 35) required at Hortham Colony, Almondsbury, near Bristol, a colony for 650 mental defectives. Salary £700–£50–£1000 p.a., less £100 p.a. for board and accommodation. A small flat is available. Previous psychiatric experience will be a recommendation. Appointment is subject to the National Health Service superannuation scheme.

Applications, with full particulars, and 3 recent testimonials, or names of 3 referees, to the Group Secretary, Hortham-Brentry Hospital Group Management Committee, 11, Regent-street, Clifton, Bristol, 8.

BURLEY-IN-WHARFEDALE, near LEEDS, YORKS. SCALEBOR PARK HOSPITAL. Applications are invited for the posts of SENIOR HOUSE OFFICERS (2). This hospital for the treatment of mental disorders (289 Beds) provides accommodation for private and Health Service patients and has a large turnover of cases (over 300 admissions in the past year). All forms of active treatment are given and Outpatient Clinics are conducted by the medical staff. Quarters for a single person are available in the hospital at a charge of £130 a year. This is a psychiatric training post with facilities for taking the University of Leeds D.P.M. No previous psychiatric experience necessary, but general hospital experience is expected.

Applications, stating age, qualifications, and experience, with the names of 3 referees, should be sent as soon as possible to the Medical Superintendent.

CAMBRIDGE. THE UNITED CAMBRIDGE HOSPITALS. Applications are invited for the post of HOUSE SURGEON (first or subsequent post) to the Orthopædic and Fracture Department at Addenbrooke's Hospital, now vacant. Salary, terms, and conditions as approved for hospital medical staff.

Applications, stating age, qualifications with dates, and nationality, and accompanied by copies of 3 recent testimonials, should be sent to the undersigned as soon as possible.

J. A. BEARDSALL, Secretary.

CAERNARVON AND ANGLESEY HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments :—

Llandudno General Hospital, Llandudno
SENIOR HOUSE SURGEON (surgical), resident.
HOUSE SURGEON (resident).

Caernarvon and Anglesey General Hospital, Bangor
HOUSE SURGEON (resident).

The appointments are for a period of 6 months. Salary and conditions of service in accordance with those approved by the Ministry of Health.

Applications, stating age, qualifications, and experience, together with the names and addresses of 2 referees, should be forwarded within 10 days of the appearance of this advertisement to the Group Secretary, Plas Gwyn, Ffriddoedd-road, Bangor, N. Wales.

CARLISLE. CUMBERLAND INFIRMARY. (322 Beds.) Applications are invited for the following resident posts for the 6 months commencing 1st October, 1952 :—

HOUSE OFFICER (orthopædic and fracture).
"SPECIALS" HOUSE OFFICER (E.N.T. and ophthalmology).
HOUSE OFFICER (gynæcology and obstetrics).

Applications, giving the names of 2 referees, should be sent to the undersigned as soon as possible.

A. PICKERING, Group Secretary,
East Cumberland Hospital Management Committee.
Cumberland Infirmary, Carlisle.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL. (Late Botleys Park War Hospital—430 Beds.) Required, RESIDENT HOUSE SURGEON for the Gynæcological and Special (E.N.T., Eyes, &c.) Departments. Salary in accordance with terms and conditions of National Health Service. Hospital within easy reach of London.

Applications, together with testimonials or names of referees, should be sent to the Physician-Superintendent, St. Peter's Hospital, as soon as possible.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL. (Late Botleys Park War Hospital—430 Beds.) Required, SENIOR HOUSE OFFICER, Orthopædic Department. Previous orthopædic experience not essential. Appointment very suitable for candidate reading for a higher qualification and is recognised by the Royal College of Surgeons for the F.R.C.S. Salary in accordance with terms and conditions of National Health Service.

Applications, together with names and addresses of referees, to Physician-Superintendent as soon as possible.

CHELTENHAM GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT SENIOR HOUSE OFFICER in Pathology. The successful applicant will work in the Group Laboratory at the Cheltenham General Hospital. Salary £670 p.a., less £130 p.a. residential emoluments. The post is tenable for 1 year in the first instance.

Applications, with the names of 3 referees, to be forwarded to the undersigned forthwith, stating age, qualifications, and experience. STANLEY T. DAVIS, Group Secretary.
General Hospital, Cheltenham.

CHESTERFIELD ROYAL HOSPITAL. Sheffield Regional HOSPITAL BOARD. Applications are invited from registered medical practitioners for the whole-time post of CASUALTY REGISTRAR to the above Hospital. The appointment is for 1 year in the first instance and may be renewed for a further year.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10, to arrive not later than 22nd September, 1952.

CHESTERFIELD ROYAL HOSPITAL. (324 Beds.) ACCIDENT AND ORTHOPÆDIC SENIOR HOUSE OFFICER required. Ministry of Health salary and conditions.

Apply— M. H. BOONE, Secretary,
Chesterfield Hospital Management Committee.

CHESTERFIELD ROYAL HOSPITAL. (324 Beds.) CASUALTY OFFICER (House Officer) required immediately at this busy General Hospital. Ministry of Health salary and conditions.

Apply— M. H. BOONE, Secretary,
Chesterfield Hospital Management Committee.

CHESTERFIELD ROYAL HOSPITAL. (324 Beds.) HOUSE SURGEON (House Officer) for general surgery required immediately. Ministry of Health salary and conditions.

Apply— M. H. BOONE, Secretary,
Chesterfield Hospital Management Committee.

CHELMSFORD. ST. JOHN'S HOSPITAL. Applications are invited for the post of RESIDENT ANÆSTHETIST (Senior House Officer) to large surgical units, for a period of 12 months, commencing immediately. The appointment will include duties at the Chelmsford and Essex Hospital a short distance away.

Applications, stating age, sex, qualifications and experience, with recent testimonials, should be sent to the Secretary, Hospital Management Committee, Chelmsford Group, Chelmsford and Essex Hospital, London-road, Chelmsford.

COVENTRY AND WARWICKSHIRE HOSPITAL. (346 Beds.) HOUSE SURGEON required to General Surgical Department (94 Beds). Vacant now. Hospital recognised for F.R.C.S. Post offers excellent experience in all types of general surgery.

Applications to the Secretary, Group 20 Hospital Management Committee, Coventry and Warwickshire Hospital, Coventry.

COTTINGHAM, E. YORKS. Senior House Officer for Raywell Sanatorium (48 Beds), and HOUSE OFFICER for Castle Hill Sanatorium (221 Beds) to work under supervision of Consultant Chest Physician. Sanatoria part of group with major thoracic surgery and mass-radiography units and laboratory facilities.

Application forms from Group Secretary, Hull B Hospital Management Committee, De la Pole Hospital, Willerby, E. Yorkshire.

CROYDON GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for appointment of ANÆSTHETIC REGISTRAR (whole-time) for Group. Duties mainly at Mayday Hospital (619 Beds), commencing October or earlier. Candidates must have experience in anæsthetics, and possession of D.A. an advantage. Candidates not precluded from visiting Hospital.

Application forms, obtainable from GEORGE A. PAINES, Secretary, Hospital Management Committee, General Hospital, Croydon, to be returned not later than 27th September.

DERBY. DERBYSHIRE ROYAL INFIRMARY. Sheffield REGIONAL HOSPITAL BOARD. Applications are invited for the resident whole-time post of SURGICAL REGISTRAR to the above Hospital, which is recognised for training in general surgery for the F.R.C.S. The appointment is for 1 year in the first instance and may be renewed for a further year.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10, to arrive not later than 29th September, 1952.

DERBY. DERBYSHIRE HOSPITAL FOR WOMEN, AND QUEEN MARY MATERNITY HOME. DERBY AREA NO. 1 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (obstetrics and gynæcology), vacant October. Duties include gynæcology at the Derbyshire Hospital for Women and the care of 26 Beds at the Maternity Home. Previous obstetric experience is desirable.

Applications, stating age, qualifications, and experience, with copies of 2 testimonials, should be forwarded immediately to the Secretary, No. 1 Hospital Management Committee, Babington-lane, Derby.

DERBY. DERBYSHIRE HOSPITAL FOR WOMEN. DERBY AREA NO. 1 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (gynæcology), vacant 2nd October. Post recognised for M.R.C.O.G. in gynæcology.

Applications, stating age, qualifications, and experience, with copies of 2 testimonials, should be forwarded immediately to the Secretary, No. 1 Hospital Management Committee, Babington-lane, Derby.

DERBY. DERBYSHIRE HOSPITAL FOR SICK CHILDREN. (84 Beds.) DERBY AREA NO. 1 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON, vacant October. Post recognised for D.C.H.

Applications, stating age, qualifications, and experience, with copies of 2 testimonials, should be forwarded immediately to the Secretary, No. 1 Hospital Management Committee, Babington-lane, Derby.

DONCASTER. HAMILTON ANNEXE, WESTERN HOSPITAL. (Recognised under the Regulations for the D.Obst. R.C.O.G.) DONCASTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of JUNIOR OBSTETRICAL HOUSE OFFICER, duties to commence end of October. The appointment is for 6 months. Salary at the rate of £350, £400, or £450 p.a., according to previous posts held, from which a deduction at the rate of £100 p.a. will be made for residential emoluments.

Applications, stating age, nationality, qualifications, and experience, and accompanied by copies of 2 testimonials, should be forwarded to the Secretary to the Committee, Doncaster Royal Infirmary.

DONCASTER ROYAL INFIRMARY. (Recognised under the regulations for the D.O.M.S.) DONCASTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of OPHTHALMIC HOUSE SURGEON at above Infirmary (330 Beds). The appointment will be in the grade of Senior House Officer and is recognised in connection with the Diploma in Ophthalmology. Salary at the rate of £670 p.a., less £100 for board, residence, &c.

Applications, stating age, education, and qualifications, and giving details of experience, should be forwarded to—

ARTHUR JONES, Secretary to the Committee.

DONCASTER ROYAL INFIRMARY. (330 Beds.) DONCASTER HOSPITAL MANAGEMENT COMMITTEE. Recognised under the regulations for the examinations of the Royal College of Surgeons. Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON. Salary at the rate of £350, £400, or £450 p.a., according to experience, from which a deduction at the rate of £100 p.a. will be made for board, residence, &c.

Applications, stating age, qualifications with dates, nationality, and present post, and accompanied by copies of 3 recent testimonials, should be forwarded to—

ARTHUR JONES, Secretary to the Committee.

Doncaster Royal Infirmary.

DAGENHAM HOSPITAL, Rainham-road South, Dagenham. There is a vacancy for the position of RESIDENT MEDICAL OFFICER (chest diseases), Junior Hospital Medical Officer status, at the above Hospital of 129 Beds for pulmonary tuberculosis, all stages. Salary £700 (for an officer appointed not less than 2 years after registration as a medical practitioner) –£50–£1000 p.a. Sound knowledge in general medicine and experience in modern treatment of tuberculosis essential. Further particulars available from the Physician-Superintendent.

Applications, stating age, qualifications, and previous experience, together with recent testimonials, to be submitted as soon as possible to—

G. AUSTIN HEPWORTH, Secretary,
Ilford and Barking Group Hospital Management Committee.
King George Hospital, Ilford.

DORKING GENERAL HOSPITAL, Horsham-road, DORKING, SURREY. REDHILL GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (resident) with some hospital experience required for duty 1st October. Firm is: visiting Consultant Physician, whole-time Physician, and resident House Physician. Excellent study opportunity for M.R.C.P.

Apply Medical Superintendent.

DUDLEY, STOURBRIDGE AND DISTRICT HOSPITAL GROUP. BIRMINGHAM REGION. Applications invited from registered practitioners for following appointments:—

The Guest Hospital Dudley (154 Beds)

HOUSE SURGEON, post now vacant.

Corbett Hospital, Stourbridge (106 Beds)

CASUALTY OFFICER, post now vacant.

SENIOR HOUSE OFFICER (resident), surgical, post now vacant. Salary £670 p.a., less £150 p.a. in respect of residential emoluments.

Wordsley Hospital, near Stourbridge (478 Beds)

SENIOR HOUSE OFFICER (resident), surgical, post now vacant. Salary £670 p.a., less £150 p.a. in respect of residential emoluments.

Applications, stating age, experience, with copies of 3 recent testimonials, to—

H. RAYMOND HURST,
Secretary to the Management Committee.

The Guest Hospital, Dudley.

EPSOM DISTRICT HOSPITAL, Dorking-road, Epsom, SURREY. (300 Beds.) RESIDENT HOUSE OFFICER (surgical) required at above Hospital. Full Consultant Staff. Post vacant 29th October, 1952, recognised by Royal College of Surgeons.

Applications, stating age, qualifications, and experience, with copies of 3 recent testimonials, should be sent as soon as possible to Group Secretary at above address.

EDINBURGH. ROYAL INFIRMARY. There will be a vacancy for a RESIDENT HOUSE OFFICER (Male) in the Venereal Diseases Department of the above Infirmary for a period of 6 months with effect from 1st October, 1952. Salary and conditions in accordance with National Health Service, regulations.

Applications to Medical Superintendent, Royal Infirmary, Edinburgh.

EDINBURGH NORTHERN GROUP OF HOSPITALS. RESIDENT ANÆSTHETIST required for 6 months commencing 1st October, 1952, to be appointed to the Eastern General Hospital in first instance. Appointment suitable for candidate proceeding to D.A. examination. Salary £350–£450 p.a., according to experience, with deduction of £100 p.a. for board and lodging.

Applications to Medical Superintendent, Western General Hospital, Edinburgh, 4.

ENFIELD, MIDDLESEX. CHASE FARM HOSPITAL. ENFIELD GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT HOUSE SURGEON (first, second, or third post), vacant 30th September, 1952, for duties with general surgical unit, which includes some orthopædics. Post recognised by the Royal College of Surgeons. 6 months appointment.

Applications, stating age, qualifications, experience, and nationality, with the names of 2 referees, to the Acting Medical Director of the Hospital by 22nd September, 1952.

ENFIELD. CHASE FARM HOSPITAL. Enfield Group HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of Locum REGISTRAR in Obstetrics and Gynæcology, vacant 1st October, for 4 weeks. Resident appointment. M.R.C.O.G. desirable but not essential.

Applications, stating age, nationality, qualifications, and previous experience, to the Acting Medical Director of the Hospital by 22nd September, 1952.

EXETER CLINICAL AREA. South-Western Regional HOSPITAL BOARD. Appointment of GENERAL PRACTITIONER SURGEON. Applications are invited from registered medical practitioners for duties equivalent to 2 3½-hour sessions in general surgery at Dartmouth and Kingswear Hospital. The practitioner appointed will be required to undertake work only at the hospital above-mentioned, and must live in, or close to, Dartmouth. Previous experience in general surgery is essential. Payment will be at the rate of £175 p.a. per weekly notional half-day.

Applications (2 copies), stating date of birth, qualifications, experience, and number of patients on National Health Service list, together with the names and addresses of 2 referees, should be sent to the Deputy Secretary, South-Western Regional Hospital Board, 5, Windsor Villas, Lockyer-street, Plymouth, not later than 29th September, 1952.

EPPING. ST. MARGARET'S HOSPITAL. (485 Beds.) Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER (anæsthetics) to fill an immediate vacancy. Busy general hospital with easy access to London. Salary on national scale, less a deduction at the rate of £130 p.a. for board and lodging.

Applications in writing, with the names of 2 referees, to Group Secretary, Epping Group Hospital Management Committee, St. Margaret's Hospital, Epping, Essex, by 20th September, 1952.

GAINSBOROUGH. JOHN COUPLAND HOSPITAL. (400 Beds.) LINCOLN NO. 1 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital. Salary and terms and conditions of service in accordance with those for medical and dental staffs employed in the Health Service. Married quarters available.

Applications, stating age, qualifications, and experience, together with copies of 3 recent testimonials, should be forwarded as soon as possible to the Group Secretary, County Hospital, Lincoln.

GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL. Applications are invited for the posts of 2 SENIOR HOUSE OFFICERS in the Psychiatric Unit of this General Hospital. The Unit of 128 Beds is under the direction of the Professor of Psychological Medicine of the University of Glasgow. The posts provide general training in psychiatry, including psychotherapy under supervision and regular case-conferences and postgraduate seminars. The posts are superannuable under the terms of National Health Service (Scotland) regulations.

Applications, with the names of 2 referees, to reach the Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Govan-road, Glasgow S.W.1, not later than 2 weeks after the appearance of this advertisement.

GRIMSBY GENERAL HOSPITAL. Grimsby Hospitals MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN. The post will become vacant on 30th September and is tenable for 6 months.

Applications, together with the names of 2 referees, should be sent to the Administrative Officer, Grimsby General Hospital.

GRIMSBY GENERAL HOSPITAL. Grimsby Hospitals MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER (Male or Female) for duties in the Casualty Department of the above Hospital.

Applications, giving full details, together with copies of 2 testimonials, to be sent as soon as possible to the Secretary, Grimsby General Hospital.

HUDDERSFIELD ROYAL INFIRMARY. (321 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER in Ophthalmology (non-resident), to commence duties immediately. Salary in accordance with the terms and conditions of service of hospital medical and dental staffs.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, should be sent to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (321 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. CASUALTY OFFICER (resident) required to commence duty on 18th September. Senior House Officer grade. Salary in accordance with the terms and conditions of service for hospital medical and dental staffs—£670 a year, less £130 in respect of residential emoluments.

Applications, together with copies of 3 recent testimonials, to be sent to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HUDDERSFIELD ROYAL INFIRMARY. (321 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty on 19th September. Salary in accordance with terms and conditions of service for hospital medical and dental staffs, with full residential emoluments.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HAVERFORDWEST. PEMBROKE COUNTY WAR MEMORIAL HOSPITAL. (162 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SURGICAL OFFICER (Senior House Officer grade). Appointment will be for 1 year and is recognised for F.R.C.S. examinations. Salary £670 p.a., and conditions of service in accordance with National agreements.

Applications, stating age, qualifications, experience, and names of 3 referees, to—

N. A. BALL, Group Secretary,
West Wales Hospital Management Committee.
Glangwili, Carmarthen.

HAVERFORDWEST. PEMBROKE COUNTY WAR MEMORIAL HOSPITAL. (162 Beds—Recognised by Royal College of Surgeons.) Applications are invited for the post of RESIDENT HOUSE OFFICER (surgical). Salary £350, £400, or £450 p.a., according to experience, less £100 p.a. for board-residence.

Applications, stating age, qualifications, experience, and nationality, with the names of 3 referees, to—

N. A. BALL, Group Secretary,
West Wales Hospital Management Committee.
Glangwili, Carmarthen.

HULL. KINGSTON GENERAL HOSPITAL. (398 Beds.) Applications are invited for the post of SENIOR SURGICAL HOUSE OFFICER (resident). Salary £670 p.a., less £130 for emoluments. Successful candidate to supervise work of 2 House Surgeons in general, orthopædic, and gynæcological work; opportunity to undertake operative work and emergency surgery. Vacancy 12th September, 1952.

Applications, with full particulars, to the Secretary, Hull A Group Hospital Management Committee.

HULL. KINGSTON GENERAL HOSPITAL. (398 Beds.) Applications are invited for the post of HOUSE OFFICER (general medicine). Salary £350, £400, or £450 p.a., according to experience. The post is resident and tenable for 6 months.

Applications, with full particulars, to be forwarded to the Secretary, Hull A Group Hospital Management Committee.

HULL ROYAL INFIRMARY. Hull A Group Hospital MANAGEMENT COMMITTEE. Applications are invited for the following posts:—

3 HOUSE SURGEONS (1 Parent Hospital, 2 Sutton Branch Hospital). Recognised for F.R.C.S.
ORTHOPÆDIC HOUSE SURGEON.
OPHTHALMIC HOUSE SURGEON. Recognised for D.O.
CASUALTY OFFICER (Senior House Officer grade).

Applications to the Hospital Secretary.

HEXHAM GENERAL HOSPITAL. (317 Beds.) Hexham AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. A vacancy will occur on 1st November, 1952, for a SENIOR HOUSE OFFICER in Anæsthetics at the above Hospital, a hospital recognised by the Royal College of Surgeons and the Royal College of Obstetricians and Gynæcologists. Salary £670 p.a.

Applications, with the names of 2 referees, should be addressed to the Group Secretary, General Hospital, Hexham, Northumberland, as early as possible.

HAYWARDS HEATH (near). CUCKFIELD HOSPITAL. MID-SUSSEX HOSPITAL MANAGEMENT COMMITTEE. RESIDENT HOUSE PHYSICIAN required for Medical and Geriatric Wards. Post vacant on 1st October. National salary scale and conditions.

Applications, stating age, qualifications, and experience, accompanied by copies of 2 recent testimonials, should be sent within 7 days of the appearance of this advertisement to the Group Secretary, Mid-Sussex Hospital Management Committee, Cuckfield Hospital, Cuckfield, Haywards Heath, Sussex.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) CASUALTY HOUSE OFFICER required. National scale of salary.

Apply to Hospital Administrator.

HASTINGS AND ST. LEONARDS. BUCHANAN HOSPITAL. (94 Beds.) SENIOR HOUSE OFFICER (urology and children's surgery) required. Post recognised for F.R.C.S. National scale salary £670 p.a., less £150 p.a. for residential emoluments.

Applications to Administrator at the Hospital.

HALIFAX. ROYAL HALIFAX INFIRMARY. (301 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (surgery). Male or Female, at the above Acute General Hospital. Salary £670 p.a., with deduction of £130 for residence, &c.

Applications, stating age, nationality, qualifications, and experience together with the names and addresses of 3 persons to whom reference may be made, should be forwarded to the undersigned as soon as possible.

R. W. RANSON, Group Secretary.

Royal Halifax Infirmary, Halifax, Yorks.

HALIFAX. ROYAL HALIFAX INFIRMARY. (301 Beds—44 Maternity.) Applications are invited for the post of OBSTETRIC HOUSE SURGEON (Male or Female) at the above Hospital. The post is recognised for the D.Obst.R.C.O.G.

Applications, stating age, nationality, qualifications, and experience, together with copies of recent testimonials, should be forwarded to the undersigned as soon as possible.

R. W. RANSON, Group Secretary.

Royal Halifax Infirmary, Halifax, Yorkshire.

HALIFAX GENERAL HOSPITAL. (425 Beds.) Applications are invited for the post of RESIDENT ANÆSTHETIST (House Officer grade) at the above Hospital. Facilities available for practical experience under guidance of Consultant Staff and there are ample opportunities for studying for D.A.

Applications, stating age, nationality, qualifications, and experience, together with copies of recent testimonials, should be forwarded to the Group Secretary at the Royal Halifax Infirmary, Halifax, Yorkshire.

HALIFAX GENERAL HOSPITAL. (425 Beds.) Applications are invited for the post of HOUSE SURGEON (House Officer grade), Male or Female, at the above Acute General Hospital.

Applications, stating age, nationality, qualifications, and experience, together with copies of recent testimonials, should be forwarded to the Group Secretary at the Royal Halifax Infirmary, Halifax, Yorkshire.

HEMEL HEMPSTEAD. WEST HERTS HOSPITAL. (170 Beds—4 Residents.) Applications are invited for the post of HOUSE SURGEON (first or subsequent post) for a term of 6 months commencing 8th October, 1952.

Applications, with full details and copies of 2 recent testimonials, should be sent to the Administrator.

HOVE GENERAL HOSPITAL, Sussex. (75 Beds—3 Resident Medical Officers.) BRIGHTON AND LEWES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (surgical), now vacant. Duties would be largely those of Resident Surgical Officer. Salary £670 p.a., less £150 for residential emoluments. Appointment for period of 6 months or 1 year.

Applications, with full particulars of qualifications, experience, &c., and enclosing names and addresses of 2 referees, should be sent to the Administrative Officer at the Hospital as soon as possible.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. South WEST MIDDLESEX HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER (first, second, or third post) required, for general medicine. Resident post.

Applications, stating age, nationality, qualifications, and experience, with copies of up to 3 recent testimonials, to Group Secretary, West Middlesex Hospital, Isleworth, Middlesex, by 23rd September, 1952.

IPSWICH. FOXHALL HOSPITAL (formerly Ipswich Sanatorium). (120 Beds—inclusive of a Thoracic Surgery Unit.) EAST ANGLIAN REGIONAL HOSPITAL BOARD. MEDICAL REGISTRAR at above Hospital. Duties will include work in the Ipswich Chest Clinic. Appointment for 1 year, renewable for second year.

Applications, stating age, qualifications, and details of present and previous appointments, together with the names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 29th September, 1952. Candidates invited to visit the hospital by direct arrangement with Hospital Management Committee Secretary, East Suffolk and Ipswich Hospital.

IPSWICH. EAST SUFFOLK AND IPSWICH HOSPITAL. (360 Beds.) Applications are invited for the post of HOUSE SURGEON to the Senior Consultant General Surgeon. House Officer post recognised for F.R.C.S.

Applications, stating age, nationality, experience, with copies of recent testimonials, to the Hospital Secretary.

IPSWICH. EAST SUFFOLK AND IPSWICH HOSPITAL. (360 Beds.) Applications are invited for the post of JUNIOR HOUSE SURGEON to the Orthopædic Consultant. The grade will be that of House Officer first, second, or third, according to experience.

Applications, stating age, sex, nationality, qualifications, and experience, with copies of recent testimonials, to the Hospital Secretary.

IPSWICH. EAST SUFFOLK AND IPSWICH HOSPITAL. (360 Beds.) CASUALTY OFFICER AND ASSISTANT HOUSE PHYSICIAN required for busy Casualty Department.

Applications to Hospital Secretary, East Suffolk and Ipswich Hospital.

IPSWICH BOROUGH GENERAL HOSPITAL. (300 Beds.) HOUSE SURGEON to General Surgeon (House Officer grade). Post, which is normally for 6 months, is recognised for F.R.C.S. examinations.

Applications, with copies of recent testimonials, to Hospital Secretary.

KINGSTON UPON THAMES. KINGSTON HOSPITAL, Wolverton-avenue. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical practitioners for the position of SENIOR HOUSE OFFICER (Orthopædic and Casualty Department), resident or non-resident. The post is vacant now. Salary and terms and conditions of service in accordance with the national scale.

Applications, stating age, qualifications, and experience, with copies of not more than 2 recent testimonials, or names of referees, should reach the Physician-Superintendent of the Hospital as soon as possible.

LIVERPOOL, 14. BROADGREEN HOSPITAL. Applications are invited for the post of HOUSE SURGEON in the Thoracic Surgical Unit. The Unit is a training centre and exceptional experience in all branches of thoracic disease is offered. Salary will be £350–£400–£450 according to experience, less £100 p.a. in respect of residential emoluments.

Applications to be forwarded to the undersigned at the above address as soon as possible.

H. BLYTHE, Group Secretary.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. LIVERPOOL EAR, NOSE AND THROAT INFIRMARY. (93 Beds.) Applications are invited for a post as REGISTRAR (E.N.T.). The appointment is for the period 1st October, 1952–30th September, 1953, but annual reappointment until completion of the normal period of training will be considered without need for further application.

Applications on forms obtainable from the undersigned should be returned by 22nd September, 1952.

A. V. J. HINDS, Secretary.
The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. LIVERPOOL EAR, NOSE AND THROAT INFIRMARY. (93 Beds.) Applications are invited for a post as SENIOR HOUSE OFFICER (E.N.T.) for the period 1st October, 1952–30th September, 1953.

Apply as soon as possible, stating age, and full particulars of qualifications and experience, to A. V. J. HINDS, Secretary.
The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ST. PAUL'S EYE HOSPITAL. (116 Beds.) As a result of an increase in the authorised establishment, applications are invited for a post as SENIOR HOUSE OFFICER in Ophthalmology for the period 1st October, 1952–30th September, 1953.

Apply as soon as possible, stating age, and full particulars of qualifications and experience, to A. V. J. HINDS, Secretary.
The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ROYAL LIVERPOOL CHILDREN'S HOSPITAL (HESWALL BRANCH). Applications are invited for an appointment as HOUSE SURGEON for the period 1st October, 1952–31st March, 1953.

Applications on forms from the undersigned should be returned as soon as possible. A. V. J. HINDS, Secretary.

The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ROYAL SOUTHERN HOSPITAL. Applications are invited for appointment as CASUALTY OFFICER for the period 1st October, 1952–31st March, 1953. The post is graded as of House Officer status.

Applications on forms from the undersigned should be returned as soon as possible. A. V. J. HINDS, Secretary.

The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ROYAL INFIRMARY, DAVID LEWIS NORTHERN HOSPITAL, ROYAL LIVERPOOL CHILDREN'S HOSPITAL. Applications are invited for appointments as RESIDENT HOUSE SURGEONS (orthopædic) for the period 1st October, 1952–31st March, 1953. Applicants appointed to posts at the Royal Infirmary and the David Lewis Northern Hospital will be required to undertake some casualty work as part of their normal duties.

Applications on forms from the undersigned should be returned as soon as possible. A. V. J. HINDS, Secretary.

The United Liverpool Hospitals, 80, Rodney-street, Liverpool, 1.

LIVERPOOL, 6. NEWSHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners (Male or Female) for the following appointments (resident or non-resident) :—

(*a*) HOUSE PHYSICIAN (dermatology). The Dermatological Department has an Outpatient Clinic dealing with approximately 50,000 attendances annually, and 180 Beds are available for inpatient treatment. The candidate appointed will be required to devote a portion of his or her time to medical wards.

(*b*) HOUSE PHYSICIAN with duties in acute and chronic medical wards.

Salaries will be £350–£400–£450 p.a. according to experience, less £100 p.a. if resident.

Applications, on forms obtainable from the undersigned, to be returned completed as soon as possible.

H. BLYTHE, Group Secretary.

Broadgreen Hospital, Liverpool, 14.

LIVERPOOL, 20. BOOTLE HOSPITAL. (119 Beds.) HOUSE SURGEON required for 6 months appointment, vacant 1st October, 1952. Ministry of Health terms and conditions of salary and service.

Application forms obtainable from the undersigned.

F. J. WATKINS, Secretary, North Liverpool Hospital Management Committee.

Walton Hospital, Liverpool, 9.

LANCASTER. ROYAL LANCASTER INFIRMARY. (230 Beds.) Applications are invited for the appointment of RESIDENT HOUSE OFFICER (surgical). The successful applicant will work with a Consultant Surgical Unit and attend at Consultative Clinics. The post is vacant and normally tenable for 6 months.

Applications, with names of 2 referees, to be addressed to the Secretary, Royal Lancaster Infirmary.

LANCASTER. ROYAL LANCASTER INFIRMARY. (230 Beds.) Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER (orthopædic). The post is recognised for F.R.C.S. examination and the successful applicant will work with an Orthopædic and Traumatic Specialist Unit. Post now vacant and normally tenable for 1 year.

Applications, with full particulars, and names of 2 referees, to be addressed to Secretary, Royal Lancaster Infirmary.

LEEDS, 12. ST. MARY'S HOSPITAL. Leeds A Group HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners (Male and Female) for the appointment of 2 HOUSE SURGEONS (obstetrics). Recognised by the Royal College of Obstetricians and Gynæcologists for Diploma. The appointments which are tenable 1st November, 1952, for a period of 6 months, are subject to the terms and conditions of service as issued by the Ministry of Health, with salary according to number of posts previously held.

Applications, stating age, qualifications, and experience, together with copy of 1 testimonial, and the names of 2 referees, should be forwarded to the Administrative Medical Officer, St. James's Hospital, Leeds, not later than 22nd September, 1952.

LEEDS. THE UNITED LEEDS HOSPITALS. Applications are invited for the appointment of REGISTRAR in Psychiatry at the General Infirmary at Leeds. The post is non-resident, and the whole of the work is carried out in conjunction with the Department of Psychiatry, University of Leeds. Opportunities for further training in psychiatry are provided. The appointment will be subject to the National Health Service (Superannuation) Regulations, 1950, and the salary will be in accordance with the terms and conditions of service of hospital medical and dental staffs.

Applications, stating age, qualifications, and details of present and previous appointments with dates, together with the names of 3 referees, should be forwarded to the Medical Secretary, Joint Registrars Committee, School of Medicine, Leeds, 2, within 10 days of publication of this advertisement.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds—General.) SOUTH WARWICKSHIRE HOSPITAL GROUP (NO. 14). Applications are invited from registered medical practitioners for the appointment of HOUSE PHYSICIAN. Post vacant on 1st October, 1952. Salary £350–£450, dependent upon experience, less £100 p.a. for residential emoluments.

Applications, with 2 recent testimonials, should be sent to the Hospital Secretary as soon as possible.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. Locum Tenens CASUALTY OFFICER required from 17th September to 14th October. Rate of salary as for Senior House Officer, £670 p.a.

Apply immediately to the Hospital Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP (NO. 14). RESIDENT HOUSE SURGEON (general surgery), first, second, or third post. Post now vacant.

Apply to the Hospital Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP (NO. 14). HOUSE SURGEON for Ophthalmic and E.N.T. Departments, tenure of post 6 months. Salary dependent on number of posts previously held and in accordance with terms and conditions of service for hospital medical and dental staffs.

Apply as soon as possible to Hospital Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds.) SOUTH WARWICKSHIRE HOSPITAL GROUP (NO. 14). Applications are invited for the appointment of RESIDENT ANÆSTHETIST. R practitioners holding first posts may apply. 6 months appointment. The post is recognised for the D.A. Salary £300 or £350, according to the previous number of appointments held, plus full residential emoluments.

Apply as soon as possible to the Hospital Secretary.

LEAMINGTON SPA. WARNEFORD GENERAL HOSPITAL. (207 Beds—General.) SOUTH WARWICKSHIRE HOSPITAL GROUP. Applications are invited from registered medical practitioners (Male or Female), for the appointment of CASUALTY OFFICER (Senior House Officer—£670), resident or non-resident. The post, vacant on 17th September, 1952, is suitable for one reading for higher qualifications, offering facilities for contact with all Specialist Units in the Hospital.

Applications, with the names and addresses of 3 referees, to be sent to the Hospital Secretary.

LEICESTER ROYAL INFIRMARY. Applications are invited for the post of HOUSE SURGEON to the E.N.T. Department for a period of 6 months commencing immediately. The post is recognised for the D.L.O. and the F.R.C.S.

Applications, stating age, experience, and qualifications, together with copies of recent testimonials, to the Secretary, No. 1 Hospital Management Committee, 38A, East Bond-street, Leicester.

LEICESTER GENERAL HOSPITAL. Applications are invited for the post of HOUSE SURGEON commencing 1st October, 1952. The post is recognised for the F.R.C.S.

Applications, stating age, experience, and qualifications, together with copies of recent testimonials, to the Secretary, No. 1 Hospital Management Committee, 38A, East Bond-street, Leicester.

LEICESTER. MARKFIELD SANATORIUM AND ISOLATION HOSPITAL. SHEFFIELD REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the resident whole-time post of REGISTRAR (chest diseases and infectious diseases) to the above Hospital, where minor thoracic surgery (T.B.) is undertaken. The duties are mainly in the Hospital, but clinic work may be undertaken under the supervision of the Consultant.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10, to arrive not later than 29th September, 1952.

LOUGHBOROUGH GENERAL HOSPITAL. (120 Beds.) Applications are invited for the vacancy of HOUSE SURGEON, commencing immediately.

Applications, stating age, qualifications, and experience, together with copies of recent testimonials, to the Secretary, Leicester No. 1 Hospital Management Committee, 38A, East Bond-street, Leicester.

LOUTH, LINCS. COUNTY INFIRMARY. (200 Beds.) Applications are invited for the post of HOUSE OFFICER (obstetrics and gynæcology) which will become vacant at this busy general hospital on 1st October, 1952. The post is resident, and a deduction of £100 p.a. will be made in respect of board, residence, &c.

Applications, giving full particulars, together with names of 2 referees, to be addressed to the Administrative Officer.

LEIGH INFIRMARY, Leigh, Lancs. (102 Beds.) Casualty OFFICER (Male or Female) required at the above Hospital. House Officer grade post, recognised for the F.R.C.S. examinations. Post vacant now.

Applications, stating age, qualifications, &c., together with the names of 2 referees, should be received by the Secretary, Wigan and Leigh Hospital Management Committee, Knowsley House, Wigan, as early as possible.

LLANELLY HOSPITAL. (164 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the resident appointment of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital, for work in the Medical and Anæsthetic Units. Post becomes vacant on 1st October.

Applications, stating age, qualifications, and experience, should be forwarded to—

O. C. HOWELLS, Secretary, Glantawe Hospital Management Committee.

St. Helen's-road, Swansea.

LLANELLY HOSPITAL. (164 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the resident post of SENIOR HOUSE OFFICER for work in the Casualty Department of the above Hospital.

Full particulars stating age, qualifications, and experience, should be addressed to—

O. C. HOWELLS, Secretary, Glantawe Hospital Management Committee.

St. Helen's-road, Swansea.

LLANELLY HOSPITAL. (164 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Applications are invited from medical practitioners for the non-resident appointment of JUNIOR HOSPITAL MEDICAL OFFICER at the above Hospital, for work mainly in the E.N.T. Department.

Applications, stating age, qualifications, and experience, with the names of 3 referees, should be forwarded to—

O. C. HOWELLS, Secretary,
Glantawe Hospital Management Committee.
St. Helen's-road, Swansea.

LUTON AND DUNSTABLE HOSPITAL, Luton, Beds. Applications are invited for the post of HOUSE PHYSICIAN, vacant 22nd September, 1952. The appointment will be for 6 months in the first instance. Salary and conditions of service in accordance with national scale.

Applications, stating age, nationality, qualifications, and experience, together with copies of 3 recent testimonials, should be sent to the Secretary, Luton and Dunstable Hospital, Luton, Beds, forthwith.

LOWESTOFT AND NORTH SUFFOLK HOSPITAL, LOWESTOFT. (99 Beds.) Applications are invited for the appointment of SENIOR HOUSE PHYSICIAN. Salary £670 p.a., less £150 for residential emoluments. Post vacant now.

Applications, stating age, qualifications, and experience, with names for reference, to Secretary.

MACCLESFIELD HOSPITAL (West Park Branch). Applications are invited for the post of RESIDENT OBSTETRIC/GYNÆCOLOGICAL HOUSE OFFICER, to become vacant 1st October, 1952. The post is recognised for the purpose of training for the D.Obst.R.C.O.G. There are 28 obstetric and 30 gynæcological beds in the unit.

Applications, stating age, nationality, qualifications, and experience, with copies of 3 recent testimonials, to be forwarded as soon as possible to the Secretary, Macclesfield and District Hospital Management Committee, "Willerby House," Cumberland-street, Macclesfield.

MAIDSTONE, KENT. PRESTON HALL HOSPITAL, BRITISH LEGION VILLAGE. Applications are invited for the appointment of SENIOR HOUSE OFFICER. Salary £670 p.a., national scale and conditions. The Sanatorium contains 330 Beds for the treatment of pulmonary tuberculosis. All modern forms of treatment are carried out including major thoracic surgery.

Applications, stating age, qualifications, and names of 2 referees to be sent as soon as possible to—

A. A. HOWICK, Secretary to the Management Committee.

MAIDSTONE. KENT COUNTY OPHTHALMIC AND AURAL HOSPITAL. (113 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE SURGEON in the E.N.T. Department of the above Hospital. There are 55 E.N.T. Beds, and 6 specialist operating sessions each week. Valuable experience is available and the post is recognised for the purposes of the F.R.C.S. Salary will be £670 a year, less £150 a year for residential emoluments.

Applications immediately to the Group Secretary, Mid-Kent Hospital Management Committee, 103, Tonbridge-road, Maidstone.

MAIDSTONE. WEST KENT GENERAL HOSPITAL. (135 Beds.) MID-KENT HOSPITAL MANAGEMENT COMMITTEE GROUP 13. Applications are invited for the appointment of HOUSE SURGEON at the above Hospital. R practitioners holding first House Officer posts may apply. 6 months appointment. Post vacant September, 1952. Salary at the rate of £350, £400, or £450, according to experience. A deduction at the rate of £100 a year is made in respect of board and lodging and other services provided.

Applications should be forwarded as soon as possible to the Administrative Officer at the Hospital.

MANCHESTER ROYAL INFIRMARY, Manchester, 13. REGISTRAR to the Department of Psychiatry, now vacant. Applicants must have held house appointments and possess a higher qualification. Whole-time appointment for 12 months, renewable.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 24th September, 1952.

F. J. CABLE, General Superintendent.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. REGISTRAR to the Group Department of Clinical Pathology. Whole-time non-resident post, tenable for 12 months, renewable, primarily intended for the training of pathologists. Applicants must have held house appointments and previous laboratory experience is desirable.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 24th September, 1952.

F. J. CABLE, Secretary to the Board of Governors.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL INFIRMARY, MANCHESTER, 13. SENIOR REGISTRAR to the Group Department of Clinical Pathology. Whole-time non-resident post tenable for 12 months, renewable. Applicants should have been qualified at least 4 years and have had at least 2 years previous experience in pathology. Facilities for training in branches of pathology will be provided both in teaching and non-teaching hospitals in Manchester.

Applications to be made on forms obtainable from the undersigned and to be returned not later than 24th September, 1952.

F. J. CABLE, Secretary to the Board of Governors.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Required, HOUSE SURGEON (first or subsequent post). Salary £350–£450 p.a., according to the number of positions previously held, less £100 p.a. for residential emoluments. Appointment of a practitioner within 3 months of qualification and subject to National Service Acts would be limited to 6 months.

Application forms available on application to—

H. R. NORTH, General Superintendent.

MANCHESTER. UNITED MANCHESTER HOSPITALS. MANCHESTER ROYAL EYE HOSPITAL. Applications are invited for RESIDENT MEDICAL STAFF (Senior House Officer grading—£670 p.a., less £100 p.a. for residential emoluments).

Application forms may be obtained from the undersigned.

H. R. NORTH, General Superintendent.

MANCHESTER. UNITED MANCHESTER HOSPITALS. SAINT MARY'S HOSPITALS. REGISTRAR in Obstetrics and Gynæcology. Applications are invited for the above appointment commencing 1st January, 1953. Salary at national scale. Initially the appointment will be for 1 year, renewable normally for a second year. The successful candidate will act during the first year as Resident Obstetric Surgeon in the obstetrical branch of the Hospital at Whitworth-street, and during the second year as Resident Surgical Officer in the gynæcological branch at Whitworth Park. The duties include some teaching, the supervision of the work of House Officers and Resident Medical Students, and very considerable clinical responsibility. Candidates must, therefore, have had fairly full previous experience in obstetrics and gynæcology. A higher qualification is not essential.

Forms of application may be obtained from the undersigned. The closing date is 4th October, 1952.

A. R. WISE, General Superintendent.

Whitworth Park, Manchester, 13.

MANCHESTER. UNITED MANCHESTER HOSPITALS. SAINT MARY'S HOSPITALS, MANCHESTER. HOUSE SURGEONS. Vacancies in the resident medical establishment for Obstetrical House Surgeons and Gynæcological House Surgeons occur as follows:

1st January, 1953–1st April, 1953.
1st July, 1953–1st October, 1953.

Applications are invited for any of these appointments from registered medical practitioners who have already completed 1 years residence in a general hospital. Previous gynæcological or obstetrical experience is not required. Applications should state whether obstetrical or gynæcological appointments are sought, or whether applicants desire to apply for either type of appointment. Normally the appointments are made 3 months in advance of the date of taking up duty, but candidates are not debarred from forwarding applications up to 1 year in advance of the date for which they wish their applications to be considered. National scale.

Application forms may be obtained from the undersigned.

A. R. WISE, General Superintendent.

Whitworth Park, Manchester, 13.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the following posts:—

Park Hospital, Davyhulme (General Hospital—426 Beds)

SENIOR HOUSE OFFICER (pædiatrics), now vacant.

HOUSE OFFICER (non-tuberculous thoracic surgery) for Manchester Regional Hospital Board Centre, the post is now vacant.

HOUSE OFFICER (general surgery) with some duties in E.N.T. work, now vacant.

The Pædiatric Unit comprises 36 Beds and Cots, including 10 non-tuberculous thoracic surgery beds. Vacancies occur periodically in the various departments at Park Hospital, and House Officers are eligible for appointment to another specialty at the end of the original term of service when such vacancies occur.

Eccles and Patricroft Hospital (General Hospital—72 Beds)

SENIOR HOUSE OFFICER, now vacant.

HOUSE OFFICER, now vacant.

The work of the Hospital is mainly surgical and there is a busy Outpatient Department.

Salaries for House Officer posts £350–£450 p.a., according to experience, £100 p.a. deduction for residential accommodation and services, 6 months appointments. The Senior House Officer appointments will be for 12 months at a salary of £670 p.a., less £130 p.a. (Eccles and Patricroft Hospital); £155 p.a. (Park Hospital), for residential accommodation and services.

Application forms from the Secretary, Park Hospital, Davyhulme, Manchester.

MANCHESTER, 9. BOOTH HALL CHILDREN'S HOS-PITAL. Recognised for D.C.H. HOUSE PHYSICIAN required. National scale and conditions.

Applications, stating age, nationality, and usual particulars, should be sent to the Medical Superintendent not later than 25th September, 1952.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of REGISTRAR (resident or non-resident) in Ophthalmology to the Burnley and District Group of hospitals, with main duties at Victoria Hospital, Burnley. The post is recognised for the purpose of the D.O.

Forms of application may be obtained from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, and should be returned with copies of 2 recent testimonials, to be received by 22nd September, 1952.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of RESIDENT REGISTRAR in Obstetrics and Gynæcology to the Wigan and Leigh Group of hospitals, with main duties at Billinge Hospital, Wigan.

Forms of application may be obtained from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, and should be returned, with copies of 2 recent testimonials, to be received by 29th September, 1952.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for the post of NON-RESIDENT REGISTRAR in E.N.T. Surgery to the Wigan and Leigh Group of hospitals, with main duties at Royal Albert Edward Infirmary, Wigan.

Forms of application may be obtained from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, and should be returned, with copies of 2 recent testimonials, to be received by 29th September, 1952.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for 2 posts of REGISTRAR in General Surgery as follows :—

(*a*) Burnley and District Group of hospitals, with main duties at Reedyford Memorial Hospital, Nelson. Modern self-contained flat available for married person.

(*b*) South Cheshire Group of hospitals, with main duties at Crewe Memorial Hospital (resident).

Forms of application may be obtained from the Senior Administrative Medical Officer, Manchester Regional Hospital Board, Cheetwood-road, Manchester, 8, and should be returned with copies of 2 recent testimonials, to be received by 22nd September, 1952.

MANCHESTER REGIONAL HOSPITAL BOARD invite applications for 4 posts of RESIDENT REGISTRAR in General Medicine as follows :—

(*a*) Bolton and District Group of hospitals, with main duties at Bolton Royal Infirmary and Bolton District General Hospital.

(*b*) North Manchester Group of hospitals, with main duties at Ancoats Hospital.

(*c*) Wigan and Leigh Group of hospitals, with main duties at Royal Albert Edward Infirmary, Wigan.

(*d*) West Manchester Group of hospitals, with main duties at Park Hospital, Davyhulme.

Forms of application may be obtained from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, and should be returned, with copies of 2 recent testimonials, to be received by 29th September, 1952.

MANSFIELD. RANSOM SANATORIUM. Nottingham NO. 5 HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the resident post of SENIOR HOUSE OFFICER. The Sanatorium contains 182 Beds for the treatment of pulmonary tuberculosis in men, women, and children, including a modern Thoracic Surgery Unit. Salary £670 p.a., less £150 for full residential emoluments which include a comfortable flat.

Applications, stating age, qualifications, and experience, and enclosing copies of 2 recent testimonials, to be sent to the Group Secretary, Harlow Wood Hospital, near Mansfield.

MEXBOROUGH. MONTAGU HOSPITAL. (123 Beds.) SENIOR HOUSE OFFICER (casualty and orthopædics). Commencing salary £670 p.a., less £140 p.a. for residential emoluments.

Applications, stating age, experience, and nationality, with names of 3 referees, to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham, Yorks, as soon as possible.

MEXBOROUGH. MONTAGU HOSPITAL. Sheffield REGIONAL HOSPITAL BOARD. Applications are invited from registered medical practitioners for the resident whole-time post of SURGICAL REGISTRAR to the above Hospital. The appointment is for 1 year in the first instance and may be renewed for a further year.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10, to arrive not later than 22nd September, 1952.

MITCHAM. WILSON HOSPITAL, Cranmer-road, MITCHAM, SURREY. ST. HELIER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications invited for appointment of RESIDENT SURGICAL OFFICER, to commence as soon as possible. Salary £350–£450 p.a., according to experience.

Applications, stating age, qualifications, and experience, with copies of 2 testimonials and the name of 1 referee, should be sent immediately to Group Secretary, St. Helier Hospital, Carshalton, Surrey.

MIDDLESBROUGH (near). POOLE SANATORIUM, NUNTHORPE. (318 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER. Salary £670 p.a., conditions of service being in accordance with the Ministry of Health regulations. The Sanatorium is a modern one having a very active Thoracic Surgical Unit.

Applications, with copies of 2 recent testimonials, should be forwarded to the Physician-Superintendent, Poole Sanatorium, Nunthorpe, Middlesbrough, immediately.

MIDDLESBROUGH. WEST LANE ISOLATION HOSPITAL. (203 Beds.) Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER. Salary £670 p.a. with a deduction of £184 p.a. for board and lodging, conditions of service being in accordance with the Ministry of Health Regulations.

Applications, with copies of 2 recent testimonials, should be forwarded to the Physician-Superintendent, West Lane Hospital, Middlesbrough, as early as possible.

MORECAMBE. QUEEN VICTORIA HOSPITAL. (100 Beds.) Applications are invited for the appointment of RESIDENT HOUSE OFFICER (surgical). The successful applicant will work with a Consultant Surgical Unit and attend at Consultative Clinics. The post is vacant and normally tenable for 6 months.

Applications with names of 2 referees, to be addressed to the Secretary, Royal Lancaster Infirmary.

NORWICH. UNITED NORWICH HOSPITALS. East ANGLIAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR (Male or Female), resident appointment in the Department of Surgery at the United Norwich Hospitals. Duties mainly at the West Norwich Hospital but also at the Norfolk and Norwich Hospital and the Jenny Lind Hospital for Children. Higher surgical qualification desirable. Appointment for 1 year, renewable for second year.

Applications, stating age, qualifications, and details of present and previous appointments, together with the names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 29th September, 1952. Candidates invited to visit the hospitals by direct arrangement with the Hospital Management Committee Secretary, Norfolk and Norwich Hospital.

MID GLAMORGAN HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments :—

Neath General Hospital, Neath (412 Beds)
HOUSE PHYSICIAN (general medicine).

Bridgend General Hospital, Quarella-road, Bridgend (364 Beds)
HOUSE SURGEON.

Neath General Hospital is recognised for the F.R.C.S., D.A., D.C.H., and D.Obst.R.C.O.G. Bridgend General Hospital is recognised for the F.R.C.S. and both hospitals have a panel of distinguished full-time and visiting Consultants.

Applications, stating age, qualifications, experience, and giving the names of 2 referees, should be addressed to the Secretary of the Committee, 8, Wind-street, Neath, immediately.

NORWICH. NORFOLK AND NORWICH HOSPITAL. (440 Beds.) Applications are invited for the appointment of JUNIOR CASUALTY OFFICER AND HOUSE SURGEON to the E.N.T. and Ophthalmic Departments (House Officer status). 6 months appointment. Salary £350, £400, or £450 according to experience, less deduction £100 p.a. for residence, &c.

Applications, stating age, experience, qualifications, with names of 2 referees, to the Secretary, Norwich, Lowestoft and Great Yarmouth Hospital Management Committee, St. Stephen's-road, Norwich.

NORFOLK. EAST NORFOLK AREA. East Anglian REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR in Chest Medicine in the above Area. Main Chest Clinic situated in Norwich. Duties include work in associated hospitals and clinics. The post offers wide experience in chest diseases. Higher medical qualification desirable and experience in chest diseases and tuberculosis essential.

Applications, stating age, qualifications, and details of present and previous appointments, together with the names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 29th September, 1952. Candidates invited to visit Clinic by direct arrangement with Hospital Management Committee Secretary at Norfolk and Norwich Hospital.

NOTTINGHAM. FIRS MATERNITY HOSPITAL. (40 Beds.) Required, RESIDENT SENIOR HOUSE OFFICER (obstetrics), post vacant 16th October, 1952. The post is recognised for D.Obst. R.C.O.G. Previous experience in obstetrics an advantage. Salary £670 p.a., less £130 p.a. for residential emoluments.

Applications, stating age, qualifications, experience, and nationality, together with copies of not more than 3 testimonials, to be sent to the Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM. CITY HOSPITAL. (821 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (paediatrics), vacant 18th October, 1952. The post is approved for the D.C.H. Salary £670 p.a., less £130 p.a. for residential emoluments.

Applications, stating age, nationality, qualifications, and experience, together with copies of not more than 3 testimonials, to be sent to the Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM. CITY HOSPITAL. (821 Beds.) Applications are invited for the post of HOUSE SURGEON. Post now vacant. Salary £350–£450 p.a., less £100 p.a. for residential emoluments.

Applications, stating age, nationality, qualifications, and experience, together with copies of not more than 3 testimonials, to be sent immediately to the Secretary, City Hospital, Hucknall-road, Nottingham.

NOTTINGHAM. CITY HOSPITAL. Sheffield Regional HOSPITAL BOARD. Applications are invited from registered medical practitioners for the resident or non-resident whole-time post of MEDICAL REGISTRAR to the above Hospital. The appointment is for 1 year in the first instance and may be renewed for a further year.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10, to arrive not later than 29th September, 1952.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER in the Department of Pathology, which becomes vacant on 1st October, 1952. Applicants must have held at least 1 Junior House appointment, and preference will be given to those with previous experience in pathology. The post affords opportunities for gaining experience in all branches of pathology. Salary and conditions of service as laid down by the Ministry of Health.

Applications, with the names of 3 referees, to be addressed to the Secretary, General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of ORTHOPÆDIC AND FRACTURE SENIOR HOUSE OFFICER. The post offers exceptional experience in traumatic surgery. Duties to commence as soon as possible. Salary £670 p.a., less £150 residential emoluments.

Applications, with copies of testimonials, should be sent as soon as possible to HENRY M. STANLEY, Secretary.

NOTTINGHAM GENERAL HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT SURGICAL OFFICER for the Casualty Department. Duties to commence on 25th October. Salary £775–£890 p.a., according to experience, less £150 emoluments. Terms and conditions of service in accordance with those laid down by the Ministry.

Applications, stating age, qualifications, and experience, together with copies of testimonials, to be sent to—

HENRY M. STANLEY, Secretary.
General Hospital, Nottingham.

NOTTINGHAM GENERAL HOSPITAL. E.N.T. Department. Applications are invited for the posts of :—
SENIOR HOUSE OFFICER.
JUNIOR HOUSE OFFICER.
Both these appointments are recognised for the D.L.O. examination, and the Senior post is recognised also for the F.R.C.S. examination. Terms and conditions of service are in accordance with the regulations of the Ministry of Health. Although the posts are normally resident, consideration will be given to any applicants who desire to live out. Duties to commence as soon as possible.

Applications, stating age, qualifications, and experience, together with copies of testimonials, should be sent to—
HENRY M. STANLEY, Group Secretary.
General Hospital, Nottingham.

NEWPORT, I.W. ST. MARY'S HOSPITAL. (Approved for pre-registration service.) ISLE OF WIGHT GROUP HOSPITAL MANAGEMENT COMMITTEE. RESIDENT CASUALTY OFFICER (Senior House Officer). Post vacant 11th October, 1952.

Applications, with 2 copy testimonials, to Chief Administrative Officer, Hospital Management Committee Headquarters, Clatterford House, Carisbrooke, I.W.

NEWPORT, MON. ROYAL GWENT HOSPITAL. (259 Beds—recognised for D.A.) Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics). The post is non-resident, and based at this Hospital, but opportunities exist for attending neighbouring hospitals, also. The successful candidate will receive a thorough training with the Consultants and the post offers extensive experience.

Apply, with the names of 2 referees, to T. A. JONES, 64, Cardiff-road, Newport, Mon.

NORTHAMPTON (near). CREATON SANATORIUM. (150 Beds.) NORTHAMPTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified registered medical practitioners for the post of SENIOR HOUSE OFFICER (resident). The Sanatorium is for the treatment of both pulmonary and non-pulmonary tuberculosis and has a thoracic surgery unit. Salary in accordance with the terms and conditions of service of hospital medical staff.

Applications, stating age, experience, and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton within 14 days of the appearance of this advertisement.

NORTHAMPTON. MANFIELD ORTHOPÆDIC HOS-PITAL. (200 Beds.) NORTHAMPTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of ORTHOPÆDIC SENIOR HOUSE OFFICER (resident). The appointment will be for 1 year. Salary £670 p.a., with a deduction of £100 p.a. for residential emoluments. The post will provide experience in a wide range of orthopædic treatment, including outpatient clinics.

Applications, stating age, nationality, qualifications, and experience, together with copies of testimonials, should be sent immediately to the Secretary, Northampton Management Committee, General Hospital, Northampton.

NORTHALLERTON. FRIARAGE AND MATERNITY HOSPITALS. NORTHALLERTON HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER in Obstetrics and Gynæcology for the above Hospitals. Previous experience in obstetrics is essential. The post will be vacant about mid-October or 1st November, will be tenable for 1 year in the first instance and is subject to the terms and conditions of service for hospital medical staff.

Applications, with copies of testimonials, or the names of 2 referees, should be addressed to the Secretary at the Friarage Hospital.

NEWCASTLE GENERAL HOSPITAL. Newcastle upon TYNE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the post of RESIDENT OBSTETRICAL HOUSE SURGEON to the Department of Obstetrics and Gynæcology (70 Beds). The duration of the appointment will be for 6 months. Salary is in accordance with the terms and conditions of the National Health Service, according to experience. The Department is recognised by the Royal College of Obstetricians and Gynæcologists for the Diplomas of M.R.C.O.G. and D.Obst.R.C.O.G., and undertakes the training of medical students in the University of Durham. The post is vacant on 1st November, 1952.

Applications should be sent without delay, together with 1 copy of 2 recent testimonials, or the names and addresses of 2 referees, to the Secretary, Newcastle General Hospital, Westgate-road, Newcastle upon Tyne, 4.

NEWCASTLE GENERAL HOSPITAL. Newcastle upon TYNE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners, Male and Female, for the resident post of HOUSE PHYSICIAN to the Pædiatric Department, tenable for 6 months from 1st November, 1952. The department is actively associated with and shares staff with the Department of Child Health of Durham University, and the post offers exceptional opportunities for gaining experience in many aspects of pædiatrics. Salary is in accordance with the terms and conditions of the National Health Service scale.

Applications, together with 1 copy of 2 testimonials, should be sent to the Secretary, Newcastle General Hospital, Westgate-road, Newcastle upon Tyne, 4.

NEWCASTLE REGIONAL HOSPITAL BOARD. East CUMBERLAND HOSPITAL MANAGEMENT COMMITTEE. (Main hospital—Cumberland Infirmary, 322 Beds.) SENIOR REGISTRAR (whole-time) required in diagnostic radiology up to 31st August, 1953, in the first instance. Salary scale during the 4-year period, £1000–£1300.

Applications, together with names and addresses of referees (preferably), or testimonials to a total of 3, to be sent to the Senior Administrative Medical Officer, "Blythswood South," Osborne-road, Newcastle upon Tyne, 2, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. New-CASTLE HOSPITAL MANAGEMENT COMMITTEE. W. J. SANDERSON ORTHOPÆDIC HOSPITAL, GOSFORTH. (141 Beds.) REGISTRAR ORTHOPÆDIC SURGEON (whole-time), resident appointment. Appointment up to 31st August, 1953, in the first instance, which may be renewed for a further year. Salary scale £775–£890 p.a.

Applications, together with names and addresses of referees (preferably), or testimonials to a total of 3, to be sent to the Senior Administrative Medical Officer, "Blythswood South," Osborne-road, Newcastle upon Tyne, 2, within 14 days.

PORTSMOUTH. SAINT MARY'S HOSPITAL, Milton-road. (74 acute medical beds.) Applications are invited for the appointment of HOUSE PHYSICIAN.

Applications, stating age, experience and qualifications, and names of 2 referees, should be submitted as soon as possible to—
E. H. HURST, Secretary,
Portsmouth Group Hospital Management Committee.
35, Grove-road South, Southsea.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the following appointments :—

Saint Mary's Hospital (general hospital, with 150 acute surgical beds and 74 acute medical beds, which is recognised for the F.R.C.S.)
1 SENIOR HOUSE OFFICER (Casualty Department) now vacant.
Infectious Diseases Hospital (310 Beds)
1 HOUSE PHYSICIAN, whose work will comprise duties in both Infectious Diseases and Tuberculosis Wards.
Queen Alexandra Hospital (124 surgical beds)
2 SENIOR HOUSE SURGEONS.
1 HOUSE SURGEON.
Chest Services (160 Beds)
1 HOUSE PHYSICIAN.

Applications, stating age, experience, qualifications, and names of 2 referees, should be submitted as soon as possible to—
35, Grove-road South, Southsea. E. H. HURST.

PORTSMOUTH. ROYAL PORTSMOUTH HOSPITAL. PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR ORTHOPÆDIC HOUSE SURGEON at the above Hospital. This is the main Orthopædic and Accident Centre of the Group, serving a population of 500,000.

Applications, stating age, experience, and qualifications, and names of 2 referees, should be submitted as soon as possible.
E. H. HURST, Group Secretary.
35, Grove-road, South, Southsea, Hants.

PERTH. COUNTY AND CITY OF PERTH GENERAL HOSPITALS. Applications are invited for the post of SENIOR HOUSE SURGEON in the General Surgical Unit, Bridge of Earn Hospital, Perthshire. The post is resident, and applicants must have been registered for not less than 2 years, of which 12 months must have been spent in House Officer appointments.

Applications, giving details of previous experience, together with the names of 3 referees, should be submitted immediately to the Medical Superintendent, County and City of Perth General Hospitals, Perth Royal Infirmary, Perth.

PERTH. COUNTY AND CITY OF PERTH GENERAL HOSPITALS. Applications are invited for the post of SENIOR HOUSE OFFICER in the Department of Anæsthetics in Bridge of Earn Hospital, Perthshire. The post is resident, and applicants must have been registered for not less than 2 years, of which 12 months must have been spent in House Officer appointments.

Applications, giving details of previous experience, together with the names of 3 referees, should be submitted to the Medical Superintendent, County and City of Perth General Hospitals, Perth Royal Infirmary, Perth.

PETERBOROUGH MEMORIAL HOSPITAL. East ANGLIAN REGIONAL HOSPITAL BOARD. SURGICAL REGISTRAR, duties primarily to be in immediate charge of busy Casualty Department but successful candidate will share other surgical duties. Post provides wide experience in casualty and general surgery. Appointment for 1 year, renewable for second year.

Applications, stating age, qualifications, and details of present and previous appointments, together with the names of 3 referees, to Secretary of Board, 117, Chesterton-road, Cambridge, by 29th September, 1952. Candidates invited to visit hospital by direct arrangement with Hospital Management Committee Secretary, Memorial Hospital, Peterborough.

PETERBOROUGH. THE MEMORIAL HOSPITAL, AND OBSTETRIC ANNEXES. Applications are invited for the position of HOUSE OFFICER (obstetrics and gynæcology). There are 56 obstetric beds, and the Unit consists of a Consultant, Registrar, and 2 House Officers, vacant 24th October, 1952.

Applications to the Secretary, Peterborough Area Hospital Management Committee, The Memorial Hospital, Peterborough, by 25th September, 1952.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL. Applications invited from registered medical practitioners for the appointments of :—
(1) RESIDENT ANÆSTHETIST, Greenbank Road Section, vacant immediately, post recognised for the D.A.
(2) HOUSE SURGEONS, Greenbank Road Section, vacant immediately, recognised for the Fellowship of the Royal College of Surgeons.
(3) SENIOR HOUSE OFFICER in Surgery, Freedom Fields Section, vacant immediately, recognised for the Fellowship of the Royal College of Surgeons.
(4) SENIOR HOUSE OFFICER in Anæsthetics, Freedom Fields Section, vacant immediately.

Applications, stating age, nationality, qualifications, and experience, together with 3 recent testimonials, to be sent to the undersigned as soon as possible.
ARTHUR R. CASH, Secretary.
7, Nelson-gardens, Devonport.

PLYMOUTH. SOUTH DEVON AND EAST CORNWALL HOSPITAL, Freedom Fields. Applications invited from duly qualified and registered medical practitioners for the appointment of SENIOR HOUSE OFFICER to Casualty and Fracture Department, vacant 1st October, 1952, for a period of 12 months which is renewable.

Applications, stating age, nationality, qualifications, and experience, with the names of 3 referees, to be sent to—

ARTHUR R. CASH, Secretary, Plymouth,
South Devon and East Cornwall General Hospital Group.
7, Nelson-gardens, Stoke, Plymouth.

PONTEFRACT AND CASTLEFORD HOSPITAL MANAGEMENT COMMITTEE. The under-mentioned posts will be vacant on the dates mentioned. In the case of resident officers an appropriate deduction will be made for emoluments.

Pontefract General Infirmary

RESIDENT SURGICAL OFFICER (graded as Senior House Officer). Salary £670 p.a. Approved training for F.R.C.S. Offers good scope for practical experience. Vacant 16th October, 1952, or sooner.

HOUSE PHYSICIAN (first or second post). Salary £350 or £400 p.a. Vacant 8th October, 1952, or sooner.

RESIDENT CASUALTY OFFICER (second or third post). Salary £400 or £450 p.a. Now vacant.

HOUSE SURGEON (first or second post). Salary £350 or £400 p.a. Approved training for F.R.C.S. Good experience. Now vacant.

Ackton General Hospital

HOUSE PHYSICIAN (first or second post). Salary £350 or £400 p.a. Will be responsible for 50 general medical beds. Good experience for acute work. Vacant 27th October, 1952.

Castleford, Normanton and District Hospital

RESIDENT SURGICAL OFFICER (graded as Senior House Officer). Salary £670 p.a. Busy general hospital. Good experience. Vacant 9th November, 1952, or sooner.

Applications with names of 2 referees to be forwarded to the Secretary, Great Northern House, Salter-row, Pontefract, Yorks.

W. BOWRING, Secretary.

REDHILL, SURREY. ROYAL EARLSWOOD INSTITUTION for Mental Defectives. ROYAL EARLSWOOD GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER (resident) at the above Institution. The appointment is in accordance with the terms and conditions prescribed by the Ministry of Health and Whitley Council, and is subject to the National Health Service superannuation regulations. Salary £700, rising to £1000 p.a., less £150 p.a. for board-residence.

Applications, stating age, qualifications, and experience, together with names of 2 referees, to be sent to the Physician-Superintendent, Royal Earlswood Institution, Redhill, Surrey, within 14 days of the appearance of this advertisement.

ROCHDALE. BIRCH HILL HOSPITAL. (General— 956 Beds.) ROCHDALE AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of SENIOR HOUSE OFFICER (anæsthetic) which is now vacant. This appointment is recognised for the D.A. and will be for 1 year. Remuneration will be at the rate of £670 p.a., and the conditions of service will be in accordance with the terms of service for hospital medical staff in the National Health Service.

Applications should be sent to—

S. HODKINSON, Group Secretary.
Central Offices, Birch Hill Hospital, Rochdale, Lancs.

ROTHERHAM. DONCASTER GATE HOSPITAL. (155 Beds.) SENIOR HOUSE OFFICER (casualty and orthopædics). Commencing salary £670 p.a., less £140 p.a. for residential emoluments.

Applications, stating age, qualifications, experience, and nationality, with names of 3 referees, to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham, as soon as possible.

ROTHERHAM. DONCASTER GATE HOSPITAL. (155 Beds.) SENIOR HOUSE OFFICER (surgery and casualty). Commencing salary £670 p.a., less £140 p.a. for residential emoluments.

Applications, stating age, experience, and nationality, with names of 3 referees, to be addressed to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham, Yorks.

ROTHERHAM. DONCASTER GATE HOSPITAL. (155 Beds), MOORGATE GENERAL HOSPITAL (368 Beds, 38 Cots). SENIOR HOUSE OFFICER, duty in Casualty, E.N.T., and Eye Departments. Commencing salary £670 p.a., less £140 p.a. for residential emoluments.

Applications, stating age, experience, and nationality, with names of 3 referees, to be addressed to the Secretary, Hospital Management Committee, "Fern Bank," Doncaster-road, Rotherham, Yorks.

RUGBY. HOSPITAL OF ST. CROSS. House Surgeon required for Orthopædic and Accident Department.

Applications, stating age, qualifications, together with copy testimonials, to be sent to the Hospital Secretary.

RUGBY. HOSPITAL OF ST. CROSS, AND ST. MARY'S HOSPITAL. HOUSE SURGEON for Obstetric (50 Beds) and Gynæcological (12 Beds) Departments required immediately.

Applications, stating age, qualifications, and experience, together with copy of testimonials, to Hospital Secretary, Hospital of St. Cross, Rugby.

SALFORD. HOPE HOSPITAL. Salford Hospital Manage- MENT COMMITTEE. SENIOR HOUSE OFFICER ANÆSTHETIST required. Salary and conditions of service as laid down by the National Health Service Act. In the theatres about 3000 operations are performed per annum. 2 Consultant Anæsthetists are available. The Hospital is recognised for the Diploma in Anæsthetics examination.

Applications, together with the names of 2 referees, should be forwarded to the Superintendent, Hope Hospital, Salford, 6, not later than 30th September, 1952.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (603 Beds.) SOUTHEND-ON-SEA HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of RESIDENT HOUSE SURGEON (recognised for F.R.C.S.), vacant 1st October, and of 6 months duration. The duties are predominantly in general surgery, but the successful applicant will also be responsible to the Consultant Orthopædic Surgeon for all orthopædic and fracture cases. Salary according to previous appointments held.

Applications, with copies of at least 2 recent testimonials, should be sent immediately to the undersigned at the General Hospital, Rochford, Essex. J. C. FIELD, Secretary.

SALISBURY. PLASTIC AND ORAL SURGERY CENTRE, ODSTOCK HOSPITAL. SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (surgical). The post is now vacant and tenable for 1 year. Experience can be gained in the plastic aspects of general surgery, maxillo-facial surgery, and burns. Applicants should have held previous house appointments. Salary and conditions of service are in accordance with the terms of medical staff in hospitals.

Applications, together with the names of 2 referees, should be sent to Group Secretary, Odstock Hospital, Salisbury, Wilts, not later than 2 weeks after the appearance of this advertisement.

SALISBURY GENERAL HOSPITAL. Salisbury Group HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER to the E.N.T. Department, for a period of 12 months from 1st October, 1952. The department has 42 Beds and is recognised for the D.L.O. and F.R.C.S.

Applications, together with the names of 2 referees should be sent to the Group Secretary, Odstock Hospital, Salisbury.

SALISBURY GENERAL HOSPITAL. Salisbury Group HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of RESIDENT HOUSE SURGEON or SENIOR HOUSE OFFICER to the Orthopædic Department. Post vacant now and is graded according to experience.

Applications, naming 2 referees, to Group Secretary, Odstock Hospital, Salisbury.

SHEFFIELD. UNITED SHEFFIELD HOSPITALS. ROYAL INFIRMARY UNIT. Applications are invited from registered medical practitioners for the post of RESIDENT SENIOR HOUSE OFFICER in Clinical Pathology, vacant November, 1952. The post offers experience in all branches of pathology and is tenable for 1 year.

Applications, stating age, qualifications, and experience, together with copy testimonials, to be addressed to the Superintendent, Royal Infirmary, Sheffield, 6.

SHEFFIELD. THE UNITED SHEFFIELD HOSPITALS. ROYAL HOSPITAL/ROYAL INFIRMARY UNITS. Applications are invited from registered medical practitioners for the post of SENIOR HOUSE OFFICER in Clinical Pathology (resident) at the Royal Hospital, at a salary of £670 p.a., less a deduction for emoluments (at present £130 p.a.). Pathological experience is not essential but candidates must have previous clinical experience. The successful candidate will be responsible for emergency pathological and blood-transfusion duties at the Hospital and will work in different branches of clinical pathology in the laboratories of The United Sheffield Hospitals.

Applications, stating age, qualifications, and experience, together with the names of 3 referees, should be forwarded immediately to— A. P. PRENTICE, Superintendent.
The Royal Hospital, West-street, Sheffield, 1.

SHEFFIELD. CITY GENERAL HOSPITAL. Sheffield REGIONAL HOSPITAL BOARD. Applications are invited for the resident whole-time post of MEDICAL REGISTRAR to the above Hospital. Experience in neurology will be considered an advantage. The appointment is for 1 year in the first instance and may be renewed for a further year.

Applications, giving age, nationality, qualifications, present and previous appointments with dates, together with names and addresses of 3 referees, should be sent to the Secretary, Sheffield Regional Hospital Board, Fulwood House, Old Fulwood-road, Sheffield, 10, to arrive not later than 29th September, 1952.

SWANSEA HOSPITAL. (403 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the resident appointment of HOUSE SURGEON.

Full particulars of age, qualifications, and experience, should be forwarded to— O. C. HOWELLS, Secretary,
Glantawe Hospital Management Committee.
St. Helen's-road, Swansea.

SWANSEA HOSPITAL. (403 Beds.) Glantawe Hospital MANAGEMENT COMMITTEE. Registered medical practitioners are invited to apply for the resident appointment of SENIOR HOUSE OFFICER in the Surgical Unit of the above Hospital.

Applications, stating age, qualifications, and experience, should be forwarded to—

O. C. HOWELLS, Secretary,
Glantawe Hospital Management Committee.
St. Helen's-road, Swansea.

SWANSEA. MORRISTON HOSPITAL. (450 Beds.) Applications are invited from registered medical practitioners for the resident appointment of SENIOR HOUSE OFFICER in the Traumatic and Orthopædic Surgical Department.

Applications, stating age, qualifications, and experience, should be addressed to the Medical Superintendent, Morriston Hospital, Swansea. O. C. HOWELLS, Secretary,
Glantawe Hospital Management Committee.

SWANSEA. MORRISTON HOSPITAL. (450 Beds.) Applications are invited from registered medical practitioners for the resident appointment of SENIOR HOUSE OFFICER in the Casualty and Orthopædic Departments.

Applications, stating age, qualifications, and experience, should be addressed to the Medical Superintendent, Morriston Hospital, Swansea. O. C. HOWELLS, Secretary,
Glantawe Hospital Management Committee.

SWANSEA. MORRISTON HOSPITAL. (450 Beds.) GLANTAWE HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the resident appointment of SENIOR HOUSE OFFICER in the Anæsthetic Department.

Applications, stating age, qualifications and experience, should be addressed to the Medical Superintendent, Morriston Hospital, Swansea. O. C. HOWELLS, Group Secretary.

ST. ALBANS CITY HOSPITAL. (425 Beds.) North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time SURGICAL REGISTRAR required at above Hospital. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, Osterhills, Normandy-road, St. Albans, Herts, by 22nd September, 1952.

ST. ALBANS CITY HOSPITAL, St. Albans. Mid Herts GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (House Officer grade) required for 1 of the 2 medical teams, for duties mainly in the acute medical wards. Post vacant now and tenable for 6 months.

Applications, giving age, qualifications, and experience, should be forwarded to the Group Secretary, Osterhills, Normandy-road, St. Albans, Herts, as soon as possible.

ST. ALBANS CITY HOSPITAL. (425 Beds.) Mid Herts GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of HOUSE SURGEON (House Officer grade) for 1 of the 2 surgical teams (recognised for the F.R.C.S.). Post tenable for 6 months.

Applications, together with the names of 2 referees, should be sent to the Group Secretary, Osterhills, Normandy-road, St. Albans, as soon as possible.

STOKE-ON-TRENT. ORTHOPÆDIC HOSPITAL, HARTSHILL. (78 Beds.) STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (orthopædics).

Apply, with copy testimonials, stating age, nationality, and full details of previous service, to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. BUCKNALL ISOLATION HOS-PITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (medical) vacant now.

Applications, with copy testimonials, and details of previous appointments held, should be forwarded to the Group Secretary, Stoke-on-Trent Hospital Management Committee, Princes-road, Stoke-on-Trent, as soon as possible.

STOCKPORT. STEPPING HILL HOSPITAL. (464 Beds.) Applications are invited for the immediate vacancy of RESIDENT HOUSE PHYSICIAN.

Applications, stating age, experience, and qualifications, together with copies of 2 testimonials, or the names of 2 referees, to be forwarded to—

H. G. PRICE, Secretary,
Stockport and Buxton Hospital Management Committee.
59B, Shaw Heath, Stockport, Cheshire.
4th September, 1952.

STOCKPORT. STEPPING HILL HOSPITAL. (464 Beds.) Applications are invited for the resident post of SENIOR HOUSE OFFICER (pathology).

⇨ Applications, stating age, experience, and qualifications, together with copies of 2 testimonials, or the names of 2 referees, to be forwarded to the undersigned, immediately.

H. G. PRICE, Secretary,
Stockport and Buxton Hospital Management Committee.
59B, Shaw-heath, Stockport, Cheshire.

SCOTLAND. WEST FIFE HOSPITALS BOARD OF MANAGEMENT. Applications are invited from suitably qualified and experienced medical practitioners for the post of NON-RESIDENT SENIOR HOUSE OFFICER (anæsthetics) at Dunfermline and West Fife Hospital, Dunfermline (115 Beds). Salary £670 p.a.

Applications, stating age, qualifications, and experience, together with the names of 3 referees, should be lodged with the Medical Superintendent, Dunfermline and West Fife Hospital, Reid-street, Dunfermline, within 30 days of the date of publication of this advertisement.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited from suitably qualified medical practitioners for the appointment of SENIOR HOUSE OFFICER in Psychiatry at Stobhill Hospital, Glasgow, N., which will be for 1 year in the first instance.

Applications, stating age, qualifications, experience, and present appointment, and giving the names of 3 referees, should be submitted not later than 20th September, 1952, to the Secretary, Board of Management for Glasgow Northern Hospitals, 13, Woodside-place, Glasgow, C.3.

SOUTHAMPTON CHEST HOSPITAL. Thoracic Surgical UNIT. Applications are invited for the appointment of RESIDENT SENIOR HOUSE OFFICER to the above Unit. Previous experience in general medicine and surgery desirable, but knowledge of thoracic surgery is not essential. The Unit comprises 70 surgical beds dealing with all types of thoracic surgery.

Applications, with copies of testimonials, should be sent as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON GENERAL HOSPITAL. (471 Beds.) RESIDENT HOUSE OFFICER (E.N.T.) required immediately. Post recognised for F.R.C.S. (Eng.) and D.L.O. examinations and provides experience in all branches of E.N.T. work. Group includes a diagnostic and distributing hearing-aid centre.

Applications, with copies of testimonials, to be submitted as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOS-PITAL (280 Beds) and SOUTHAMPTON GENERAL HOSPITAL (459 Beds). Applications are invited for the whole-time post of SENIOR HOUSE OFFICER (E.N.T.), now vacant. The post is recognised for the F.R.C.S. (Eng.) and D.L.O. examinations, providing experience in all branches of E.N.T. work, including audiometry. The group includes a diagnostic and distributing Hearing-aid Centre. Occasional work at other hospitals may be required.

Applications, with copies of 3 recent testimonials, should be forwarded as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (280 Beds.) CASUALTY OFFICER (Senior House Officer grading) required immediately.

Applications, with copies of testimonials, to be submitted as soon as possible to the Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

TILBURY AND RIVERSIDE GENERAL HOSPITAL. ORSETT BRANCH. Applications are invited from registered medical practitioners for the post of OBSTETRIC HOUSE SURGEON at the above Hospital, Male or Female, resident. 6 months appointment in the first instance. Post becomes vacant on 25th September, 1952.

Applications, together with copies of not more than 3 recent testimonials, should be forwarded to the undersigned as soon as possible. G. E. WHYTE, Group Secretary,
South East Essex Hospital Management Committee.
Thurrock Hospital, Grays, Essex.

TILBURY AND RIVERSIDE GENERAL HOSPITAL. TILBURY BRANCH. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (resident) at the above Hospital. The appointment will be for 6 months in the first instance and the post is now vacant.

Applications, together with copies of not more than 3 recent testimonials, should be forwarded to the undersigned as soon as possible. G. E. WHYTE, Group Secretary,
South East Essex Hospital Management Committee.
Thurrock Hospital, Grays, Essex.

TILBURY AND RIVERSIDE GENERAL HOSPITAL. TILBURY BRANCH. SOUTH EAST ESSEX HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER to the Casualty, Orthopædic and Fracture Department, Tilbury Hospital. The post offers practical experience in the treatment of all types of surgery. The post, which is now vacant, will be for 6 months in the first instance.

Applications, together with copies of not more than 3 recent testimonials, should be forwarded to the undersigned as soon as possible. G. E. WHYTE, Group Secretary.
Thurrock Hospital, Grays, Essex.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE PHYSICIAN required to the Special Unit for Research in Juvenile Rheumatism. Post vacant 4th November and offers scope for those interested in research, pædiatrics, rheumatology, or cardiology, and previous experience in 1 of these is desirable.

Applications, stating age, qualifications with dates, and experience, together with copies of 2 testimonials, should be sent to the Hospital Secretary.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE SURGEON to the Unit of Obstetrics and Gynæcology required for post vacant on 4th November. The post is recognised for the M.R.C.O.G. and preference will be given to candidates who have had previous experience in midwifery and gynæcology. Salary on national scale.

Applications, stating age, qualifications with dates, and experience, together with copies of 2 testimonials, should be sent to the Hospital Secretary, by 19th September.

TREDEGAR. ST. JAMES HOSPITAL. Resident Senior HOUSE OFFICER (Male or Female), required at above Hospital, for duties primarily on the acute and chronic sick wards (116 Beds). Term of appointment 12 months. Salary £670 p.a., less an agreed deduction for full residential emoluments. Medical establishment comprises Visiting Physicians, Geriatrician, and Obstetrician, together with resident Senior Hospital Medical Officer and Junior House Officer.

Apply to the Hospital Management Committee Secretary, District Hospital, St. Martins-road, Caerphilly.

TUNSTALL. BURSLEM, HAYWOOD AND TUNSTALL WAR MEMORIAL HOSPITAL. STOKE-ON-TRENT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE OFFICER (surgical).

Apply, with copy testimonials, stating age, nationality, and full details of previous service, to the Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

TRURO. ROYAL CORNWALL INFIRMARY. (General Hospital—212 Beds ; 8 Residents.) WEST CORNWALL HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR RESIDENT HOUSE OFFICER to the Orthopædic and Traumatic Department, which falls vacant on 6th December, 1952. This is a large and busy centralised Unit with 2 Consultants, 64 Beds, and Outpatients' Departments which deal with the whole of the West Cornwall Area. The post is tenable for 1 year.

Applications, stating age, nationality, qualifications, and experience, and accompanied by copies of 2 recent testimonials, should be forwarded to the Hospital Secretary, Royal Cornwall Infirmary, Truro, without delay.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS-PITAL. HOUSE OFFICER (anæsthetics) vacant 16th September, 1952. The hospital is recognised for the D.A.

Applications, with copies of 2 testimonials, should be sent to the Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. HOUSE PHYSICIAN to Maternity Department, vacant 20th September, 1952. Hospital is recognised by the Royal College.

Applications, with copies of 2 testimonials, should be sent to the Secretary.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOSPITAL. Locum REGISTRAR in Anæsthetics (Senior grade preferred) required. The post is non-resident and preference will be given to applicants holding the D.A.

Apply to Secretary, Royal Hampshire County Hospital.

WAKEFIELD. THE GENERAL HOSPITAL, Park Lodge-lane, WAKEFIELD. (160 Beds.) HOSPITAL MANAGEMENT COMMITTEE NO. 9 WAKEFIELD A GROUP. Applications are invited for the appointment of a SENIOR HOUSE OFFICER in General Surgery at the above Hospital. Terms and conditions of service are in accordance with the National Health Service Act and regulations thereunder.

Application forms may be obtained immediately from the Medical Superintendent. W. READ, Group Secretary.

WAKEFIELD. PINDERFIELDS GENERAL HOSPITAL. Applications invited for the appointment of JUNIOR HOSPITAL MEDICAL OFFICER to General Medical Unit (70 Beds). Salary scale £700–£50–£1000 p.a., less a charge at the rate of £130 p.a. if resident.

Address applications, with full particulars of qualifications, &c., and names and addresses of 2 persons for reference, to—

G. L. BANNER, Group Secretary.

Victoria Chambers, Wood-street, Wakefield.

WARRINGTON GENERAL HOSPITAL. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (obstetrics and gynæcology). This post is recognised for the D.Obst.R.C.O.G.

Applications, stating age, qualifications with dates, and details of experience, together with copies of recent testimonials, should be sent immediately to the Group Secretary, Warrington and District Hospital Management Committee, General Hospital, Warrington.

WARRINGTON GENERAL HOSPITAL. (388 Beds.) There is a vacancy at the above Hospital for a HOUSE SURGEON (Male or Female). The scale of salary will be in accordance with the National Health Service terms and conditions. The staffing of the Surgical Unit consists of a Senior Registrar, Senior House Officer, and 2 House Surgeons. The post offers a comprehensive training in surgery.

Apply, giving full particulars to—

H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

WARRINGTON INFIRMARY. (172 Beds.) Applications are invited for a RESIDENT HOUSE OFFICER (Male or Female). The main duties will be those of House Physician but the appointed person will be required to assist in E.N.T. and other duties. Salary will be £350–£450 p.a., less a deduction of £100 for full residential emoluments.

Applications should be sent to—

H. L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

WARRINGTON INFIRMARY. (172 Beds.) Applications are invited for a vacancy at the above Hospital for a RESIDENT HOUSE SURGEON. Salary will be £350–£450 p.a., less a deduction of £100 for full residential emoluments.

Applications should be sent to—

H. L. BOOT, Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR in Obstetrics and Gynæcology to cover the Newport and East Monmouthshire Hospital Management Committee. The successful candidate will be based at the Royal Gwent Hospital, Newport, Mon. (259 Beds), and attend neighbouring Hospitals. Accommodation for a lady doctor or single man is available at the County Hospital, Griffithstown (234 Beds). The post will be subject to review at the end of the first year.

Forms of application should be obtained from the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Temple of Peace and Health, Cathays Park, Cardiff, within 14 days of appearance of this advertisement.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of a REGISTRAR in General Medicine to serve the Clwyd and Deeside Hospital Management Committee. The successful candidate will be based at the Royal Alexandra Hospital, Rhyl (138 Beds). The post is non-resident and will be subject to review at the end of the first year.

Forms of application should be obtained from the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 14 days of appearance of this advertisement.

WORTHING HOSPITAL. (221 Beds.) Worthing Group HOSPITAL MANAGEMENT COMMITTEE. Additional appointment. Applications are invited for the post of ANÆSTHETIST REGISTRAR. Preference will be given to candidates holding Diploma in Anæsthetics.

Forms of application are obtainable from the undersigned and must be returned within 14 days from the appearance of this advertisement. A. V. OAKTON, Group Secretary,

Worthing Group Hospital Management Committee.
129, Brighton-road, Worthing, Sussex.

WOKING VICTORIA HOSPITAL, Woking, Surrey. (72 Beds.) SENIOR HOUSE OFFICER (temporary) required. Surgical and medical duties. Resident or non-resident. Salary as laid down by Ministry of Health.

Apply with testimonials to Hospital Secretary at above address.

WOKING VICTORIA HOSPITAL, Woking, Surrey. (72 Beds.) HOUSE OFFICER (surgical and medical duties) required. Resident preferred, non-resident considered. Salary and conditions of service as laid down by Ministry of Health.

Apply, with testimonials, to Assistant Secretary.

WIGAN. ROYAL ALBERT EDWARD INFIRMARY. (198 Beds.) WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE. HOUSE PHYSICIAN (resident) required at the above hospital. House Officer grade post, vacant 30th September, 1952.

Applications, stating age, qualifications, and details of previous employments, together with the names of 2 referees, should be forwarded to the Secretary, Wigan and Leigh Hospital Management Committee, Knowsley House, Wigan, as early as possible.

WORKSOP, NOTTS. VICTORIA HOSPITAL. (127 surgical beds.) WORKSOP AND RETFORD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duties immediately. Appointment for 6 months in first instance. Salary at rate of £350–£450 according to number of posts held. A deduction of £100 p.a. will be made in respect of residential emoluments.

Applications, stating age, qualifications, nationality, together with copies of recent testimonials, to be forwarded to the Secretary, Worksop and Retford Hospital Management Committee, Victoria Hospital, Worksop.

WORKSOP, NOTTS. KILTON HOSPITAL. (70 acute medical beds which include medical, dermatological, and pædiatric.) HOUSE PHYSICIAN required to commence duties immediately. Appointment for 6 months in first instance. Salary at rate of £350–£450, according to number of posts held. A deduction of £100 p.a. will be made in respect of residential emoluments.

Applications, stating age, qualifications, nationality, together with copies of recent testimonials, to be forwarded to the Secretary, Worksop and Retford Hospital Management Committee, Victoria Hospital, Worksop.

WOLVERHAMPTON HOSPITAL MANAGEMENT COMMITTEE GROUP NO. 16, BIRMINGHAM REGION.

The Royal Hospital, Wolverhampton (an Associated Hospital of the University of Birmingham Medical School)
SENIOR HOUSE OFFICER (Fracture and Orthopædic Department), vacant now.
HOUSE OFFICER (Fracture and Orthopædic Department), vacant now.
HOUSE OFFICER (Ear, Throat and Nose Department), vacant now. Salary £450 p.a.

Wolverhampton and Midland Counties Eye Infirmary
(Recognised for the full course of instruction for admission to the D.O.)
SENIOR HOUSE OFFICER, vacant now.

New Cross Hospital, Wolverhampton
HOUSE OFFICER (general surgery), vacant now.
2 HOUSE OFFICERS (medical), vacant now.

Applications, with copies of 3 recent testimonials, to be sent to W. COCKBURN, Group Secretary.
The Royal Hospital, Wolverhampton.

WREXHAM. MAELOR GENERAL HOSPITAL. (513 Beds.) WREXHAM, POWYS, AND MAWDDACH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE SURGEON at the above Hospital, to commence immediately. The appointment is recognised for the Diploma of F.R.C.S. (Eng. and Edin.). Salary will be at the rate of £350, £400, or £450 p.a., according to experience, less £100 p.a. for full residential emoluments.

Applications, stating age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, should be addressed to—

WILLIAM JONES, Secretary, Wrexham,
Powys, and Mawddach Hospital Management Committee.
Maelor General Hospital, Crocsnewydd-road, Wrexham.

WREXHAM. WAR MEMORIAL HOSPITAL. (170 Beds.) WREXHAM, POWYS, AND MAWDDACH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of HOUSE SURGEON at the above Hospital, to commence immediately. Salary will be at the rate of £350, £400 or £450 p.a. according to experience, less £100 p.a. for full residential emoluments.

Applications, stating age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, should be addressed to—

WILLIAM JONES, Secretary, Wrexham,
Powys, and Mawddach Hospital Management Committee.
Maelor General Hospital, Crocsnewydd-road, Wrexham.

WREXHAM. WAR MEMORIAL HOSPITAL. (170 Beds.) WREXHAM, POWYS, AND MAWDDACH HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of HOUSE PHYSICIAN at the above Hospital. The appointment will be for 6 months and will commence immediately. Salary will be at the rate of £350–£450 p.a., according to experience, less £100 p.a. for full residential accommodation.

Applications, stating age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, should be addressed to—

WILLIAM JONES, Secretary, Wrexham,
Powys, and Mawddach Hospital Management Committee.
Maelor General Hospital, Croesnewydd-road, Wrexham.

NEW YORK CITY. State University of New York College of Medicine at New York City in affiliation with Kings County Hospital now offers a 2-year RESIDENCY in Anesthesiology.

For further information write to MEREL H. HARMEL, M.D.
Kings County Hospital, 451, Clarkson-avenue,
Brooklyn, N.Y.

NEW YORK. ALBANY HOSPITAL. Anesthesiology RESIDENCY. Approved for 1 or 2 years; for graduates of approved medical schools who have completed 1 year of an approved internship. Medical college affiliation.

Apply to J. GERARD CONVERSE, M.D.
Albany Hospital, Albany 1, New York, U.S.A.

NEW YORK. ALBANY HOSPITAL. Immediate opportunity ASSISTANT RESIDENCY PEDIATRICS at Albany Hospital, a 750-Bed private Institution associated directly with Albany Medical College. Uniforms, laundry, room, and food, plus $600 annually.

Send applications to— Dr. JOHN K. MENEELY, Jr., Director of House Staff Education.
Albany Hospital, Albany, New York, U.S.A.

Public Appointments

DUBLIN. LOCAL APPOINTMENTS COMMISSION, position vacant. Leitrim County MEDICAL OFFICER. Salary £1200–£30–£1440.

Application forms and particulars from the Secretary, 45, Upper O'Connell-street, Dublin. Latest time for receiving completed application forms : 5 P.M. on 23rd September, 1952.

FACTORY DOCTORS: Factories Acts, 1937 and 1948. The following appointments as Appointed Factory Doctor under the Factories Acts, 1937 and 1948, are vacant. Applications should be sent to the Chief Inspector of Factories, 8, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of application*
BARGOED	GLAMORGAN ..	27TH SEPTEMBER, 1952
SOUTHAMPTON ..	SOUTHAMPTON ..	27TH SEPTEMBER, 1952

MONMOUTHSHIRE COUNTY COUNCIL. The Council invite applications from duly qualified medical practitioners for the appointment of ASSISTANT MEDICAL OFFICER. Possession of the D.P.H. or similar qualification would be an advantage. The duties will mainly be the medical inspection and treatment of school-children and infant welfare work. The salary will be at the rate of £850 p.a., rising by increments of £50 to a maximum of £1150 p.a. The successful candidate will be required to act under the direct supervision of the County Medical Officer ; to devote whole-time to the work of the County Council, and to reside in such place as the County Council may determine. The post will be subject to the provisions of the National Health Service superannuation regulations, and to a satisfactory medical examination.

A schedule of duties to be performed, together with conditions of appointment and a form of application, can be obtained from the County Medical Officer to whom applications, accompanied by copies of not more than 3 testimonials, are to be sent by 30th September, 1952.

VERNON LAWRENCE, Clerk of the Council.
County Hall, Newport, Monmouthshire.

MIDDLESEX COUNTY COUNCIL. County Health DEPARTMENT.

(*a*) SENIOR ASSISTANT MEDICAL OFFICER required, in Area 8 (Hayes/Harlington, Ruislip, Northwood, Uxbridge, Yiewsley/West Drayton). Administrative and clerical duties in school health and local health services. Must be prepared, if required, to undertake also duties of Medical Officer of Health or Deputy of one or more of County Districts in area, in which case salary amended as appropriate nationally negotiated scale. Salary £1150–£50–£1400 p.a. inclusive.

(*b*) ASSISTANT MEDICAL OFFICER in Area 2 (Southgate, Wood Green, Friern Barnet, Potters Bar). Duties include supervision of health of school-children, mothers, and young children attending health clinics, and routine medical inspection at schools. D.P.H., C.P.H., D.C.H., or experience in these branches of public health work an advantage. Salary £850–£50–£1150 p.a. inclusive.

Established, whole-time posts. Subject to medical assessment and prescribed conditions.

Apply (no forms), stating age, qualifications, experience, and names of 2 referees to Area Medical Officer (*a*) Local County Offices, High-street, Uxbridge (*b*) Town Hall, Palmers Green, London, N.13, by 27th September (quoting L.184.L.). Canvassing disqualifies.

C. W. RADCLIFFE, Clerk of the County Council.

NOTTINGHAM. CITY OF NOTTINGHAM HEALTH DEPARTMENT. Appointment of SENIOR MEDICAL OFFICER. Applications are invited for this appointment from medical practitioners of wide experience. The successful candidate will be mainly concerned with the drawing up of a scheme for the care of older people, and later will organise, initiate, and conduct such a scheme. He will undertake other duties, including epidemiology, in the Health Department, as decided by the Medical Officer of Health, under whose general direction he will work. The post is superannuable and subject to medical examination. The salary scale is £1250–£50–£1650 p.a. ; commencing salary according to experience and qualifications.

Details of the duties, conditions of appointment, and forms of application, may be obtained from the undersigned to whom they should be returned not later than 5th October, 1952, accompanied by the names of 3 persons to whom reference may be made.

Guildhall, Nottingham. T. J. OWEN, Town Clerk.

SUDAN GOVERNMENT. The Ministry of Health requires the services of ANÆSTHETIST AND LECTURER in Anæsthetics. Candidates should not be over the age of 40 years and should have specialist experience in anæsthetics. Appointment will be on short-term contract (with bonus) for a period not exceeding 6 years. Starting rate at age 34 is £E.2500 p.a. with annual increments. A lower rate of pay than £E.2500 will be given to a candidate below the age of 34 years. These rates are consolidated and no cost-of-living allowance is payable. The contract will provide for a bonus of 1 months salary for each year of service from appointment, subject to a maximum of 6 months salary. There is at present no income-tax in the Sudan. Free passage on appointment.

Full particulars and application forms may be obtained on application to Sudan Agent in London, Wellington House, Buckingham-gate, London, S.W.1. Please mark envelope "Anæsthetist."

NORTHAMPTONSHIRE COUNTY COUNCIL. Applications are invited for the whole-time appointment of ASSISTANT MEDICAL OFFICER for Maternity and Child Welfare and School Medical Inspection on the salary scale of £850–£50–£1150 p.a., in accordance with the Industrial Court Award No. 2285. Travelling and subsistence allowances will be paid on the scale from time to time approved by the Council. Candidates should possess special knowledge of, and experience in, maternity and child welfare work, and preference will be given to those who hold the Diploma in Child Health, and have been approved by the Minister of Education for the examination and ascertainment of educationally sub-normal pupils. The Officer appointed will work under the direction of the County Medical Officer of Health. The appointment will be subject to the Local Government Superannuation Acts, and will be determinable by 3 months notice on either side.

Applications, stating age, qualifications, and experience, with the names of 2 referees, should reach the undersigned not later than 4th October, 1952.

J. ALAN TURNER, Clerk of the County Council.
County Hall, Northampton, 5th September, 1952.

NATIONAL COAL BOARD. Applications are invited from registered medical practitioners for a full-time appointment as MEDICAL OFFICER to the Central East Area (which covers Bathgate/Shotts/West Calder districts) of the Scottish Division. Duties will embrace the usual functions of industrial medical officer, including : (*a*) pre-employment and other medical examinations ; (*b*) organisation and supervision of first-aid and nursing services ; and (*c*) advice to management. Candidates should have had experience in general practice and/or in the field of preventive and industrial medicine. Knowledge of the coalmining industry will be an advantage. Salary will be within the range of £1250–£1900 p.a. according to qualifications, age, and experience. The successful candidate will require to pass a medical examination. The post is superannuable.

Applications, giving full particulars of age, qualifications, experience, and present appointment, and salary, together with 3 references, should be sent to the Establishments Officer, National Coal Board, 1, Eglinton-crescent, Edinburgh, 12, within 14 days of the publication of this advertisement. Original testimonials should not be sent.

WESTMINSTER CITY COUNCIL AND HOLBORN BOROUGH COUNCIL. Joint appointment of PRINCIPAL ASSISTANT MEDICAL OFFICER OF HEALTH (permanent appointment). Salary £1250–£50–£1400 p.a. Post is superannuable. Applicants to be registered medical practitioners and to hold a registered Public Health qualification ; age not to exceed 45 years. The person appointed will act as joint Principal Assistant Medical Officer of Health for the two Boroughs and (subject to the approval of the Minister of Health) as deputy in the absence of both Medical Officers of Health at the same time. His services will be allocated in the proportion of three-fourths to Westminster ; one-fourth to Holborn.

Applications, marked "Principal Assistant Medical Officer of Health," stating name, address, age, war service, qualifications, present and past appointments, experience, whether related to any member or senior officer of either Council, with copies of 3 recent testimonials, must be received by the Town Clerk of the City of Westminster (City Hall, Charing Cross-road, W.C.2) by 4th October, 1952. Canvassing will disqualify.

PARKER MORRIS, Town Clerk, City of Westminster.
C. F. S. CHAPPLE, Town Clerk, Borough of Holborn.
26th August, 1952.

YORKSHIRE. COUNTY COUNCIL OF THE WEST RIDING OF YORKSHIRE. Joint appointments of SENIOR ASSISTANT COUNTY MEDICAL OFFICERS. Applications are invited from registered medical practitioners (Men or Women) for posts in the following areas :—

Division No. 3. Keighley Corporation, and the West Riding County Council.

Division No. 4. Baildon, Bingley, Denholme, and Shipley Urban District Councils, and the West Riding County Council.

Division No. 5. Pudsey Corporation, Aireborough and Horsforth Urban District Councils, and the West Riding County Council.

Division No. 8. Harrogate Corporation, Knaresborough Urban District Council, Nidderdale Rural District Council, and the West Riding County Council.

Division No. 11. Castleford and Normanton Urban District Councils, and the West Riding County Council.

Division No. 19. Todmorden Corporation, Hebden Royd, Ripponden, and Sowerby Bridge Urban District Councils, Hepton Rural District Council, and the West Riding County Council.

Division No. 22. Hoyland Nether, Penistone, and Stocksbridge Urban District Councils, Wortley Rural District Council, and the West Riding County Council.

The Senior Assistant County Medical Officer will be on the staff of the County Medical Officer's Department but will work under the administrative direction of the Divisional Medical Officer and the Medical Officer of Health, who is responsible for the day-to-day administration of practically all public health matters in the Division, and the post is suitable for medical officers who hold the D.P.H. and wish to obtain further experience in the field of public health. The duties of the office will be mainly clinical in the School Health and Infant Welfare services, but in addition to these duties the person appointed will be required to act for the Divisional Medical Officer and Medical Officer of Health in his absence. The scale of salary is £950 p.a. rising by annual increments of £50 to £1250 p.a. Travelling and subsistence allowances according to the County Council's scale are payable in addition to salary. The posts are superannuable and successful applicants will be required to pass a medical examination as to physical fitness.

Forms of application can be obtained from the undersigned, to whom they should be returned within 21 days of the appearance of this advertisement.

J. WOOD-WILSON, Deputy County Medical Officer.
County Hall, Wakefield.

YORKSHIRE. COUNTY COUNCIL OF THE WEST RIDING OF YORKSHIRE. Appointment of ASSISTANT COUNTY MEDICAL OFFICERS. Applications are invited from registered medical practitioners (Men or Women) for posts in the following areas :—

Division No. 9. Wetherby and Tadcaster Rural Districts.
Division No. 11. Castleford and Normanton Urban Districts.
Division No. 18. Brighouse Borough, Elland, and Queensbury and Shelf Urban Districts.
Division No. 20. Colne Valley, Holmfirth, Denby Dale, Meltham, and Kirkburton Urban Districts.
Division No. 25. Darfield, Dodworth, Wombwell, and Worsborough Urban Districts.
Division No. 28. Doncaster Rural and Tickhill Urban Districts.

The Assistant will be on the staff of the County Medical Officer's Department, but will work under the administrative direction of the Divisional Medical Officer for the Area. The duties will be mainly clinical in the School Health and Infant Welfare services, but other health duties may be included by the Divisional Medical Officer. The scale of salary is £850 p.a. rising by annual increments of £50 to £1150 p.a. A Diploma in Child Health, although not essential, will be an advantage. Travelling and subsistence allowances according to the County Council's scale are payable in addition to salary. The posts are superannuable and successful applicants will be required to pass a medical examination as to physical fitness.

Forms of application can be obtained from the undersigned, to whom they should be returned within 21 days of the appearance of this advertisement.

J. WOOD-WILSON, Deputy County Medical Officer.
County Hall, Wakefield.

ORKNEY COUNTY COUNCIL. North-Eastern Regional HOSPITAL BOARD, SCOTLAND. Applications are invited from registered medical practitioners who are registered in the Medical Register as the holders of a Diploma in Sanitary Science, Public Health or State Medicine for the joint appointment of MEDICAL OFFICER OF HEALTH AND GROUP HOSPITALS OFFICER for the County of Orkney. Applicants must be qualified in the clinical and domiciliary care of tuberculosis, infectious diseases, and chronic sick and have experience in public health duties and functions and of administrative work in hospitals, sanatoria, &c. The salary attached to the combined post, which is superannuable, is £1600 p.a., rising by annual increments of £50 to £1800 p.a. A house is available in Kirkwall at an annual rental of £50 plus occupiers' rates and may be occupied by the holder of the combined post for the duration of his appointment.

Full particulars may be obtained from the County Clerk, County Offices, Kirkwall, Orkney, with whom applications, testimonials, and the names of 2 referees, should be lodged by 11th October, 1952.

DOUGLAS M. WOOD, County Clerk.
County Offices, Kirkwall, 4th September, 1952.

JOHN N. MCCONACHIE, Secretary.
North-Eastern Regional Hospital Board, Aberdeen.

ROSCOMMON COUNTY COUNCIL. St. Patrick's REGIONAL CHEST HOSPITAL, CASTLEREA. Applications are invited from suitably qualified persons for the filling of 1 or more posts as Temporary Whole-time LABORATORY TECHNICIANS at St. Patrick's Regional Chest Hospital, Castlerea. Remuneration £360 p.a. inclusive. Applicants must be members of the Institute of Medical Laboratory Technology.

Full particulars as to qualifications and duties and forms of application may be obtained from the undersigned. Latest time for receipt of applications is 5 P.M. on Friday, 26th September, 1952.

M. A. GERAGHTY, Deputy County Secretary.
Courthouse, Roscommon, 5th September, 1952.

SHEFFIELD EDUCATION COMMITTEE. Applications are invited from duly qualified medical practitioners (Men and Women) for appointment as ASSISTANT SCHOOL MEDICAL OFFICER. Special consideration will be given to the applications of candidates who have had experience in the treatment of children. Possession of the D.P.H. or D.C.H. qualifications will be an advantage. Salary £850 p.a. rising to £1150 p.a. by annual increments of £50. Superannuable post. Subject to satisfactory medical examination.

Application forms and particulars of the appointment obtainable on receipt of stamped addressed foolscap envelope, to be returned to the Director of Education, Leopold-street, Sheffield, by 4th October, 1952.

ROYAL NAVAL MEDICAL SERVICE

Candidates are invited for service as Medical Officers in the Royal Navy—preferably below 28 years.

They must be British subjects whose parents are British subjects, and be medically fit. No examination will be held but an interview will be required.

Initial entry will be for 4 years' short service after which gratuity of £600 (tax free) is payable, but permanent commissions are available for selected short-service officers.

Officers entered on or after 1st January, 1951, will be eligible to be considered for ante-dates of seniority up to 2 years for service in recognized civil hospitals, etc.

For full details apply MEDICAL DIRECTOR-GENERAL, Admiralty, S.W.1.

PORTSMOUTH. CITY OF PORTSMOUTH. Public HEALTH DEPARTMENT. Applications are invited from registered medical practitioners for the appointment of ASSISTANT MEDICAL OFFICER OF HEALTH. Preference will be given to candidates possessing the D.P.H. The doctor appointed will be responsible to the Medical Officer of Health for the operation of the Department's Immunisation and Vaccination Service and the Disinfestation (Scabies and Pediculosis) Clinic, and will also be required to carry out any other duties as he may direct. The salary scale is £850–£50–£1150, and regard will be had to previous service when fixing the commencing salary. The successful applicant will be required to pass a medical examination.

Application forms may be obtained from, and should be returned to, the Medical Officer of Health, 1, Western-parade, Portsmouth, not later than Saturday, 20th September, 1952.

V. BLANCHARD, Town Clerk.

City Council Chambers, 1, Clarence-parade, Portsmouth.

Hospital Services : Non-Medical Appointments

ST. GEORGE'S HOSPITAL, S.W.1. Required for Hæmatology Department, SHORTHAND-TYPIST AND SECRETARY. Some knowledge of laboratory or blood-transfusion organisation would be an advantage. Salary to commence £360 p.a. at age 26 or over.

Apply in writing to Chief Clerk.

Miscellaneous

To non-professional posts the Notification of Vacancies Order 1952 applies

Assam. A British Medical Officer is required for a group of Tea Estates ; age 28 to 36 years ; tropical clinical and hygiene experience an advantage. Basic salary £1350 p.a. for 3-year agreement which is renewable. Dearness allowance £315 p.a., plus marriage and children's allowance ; car allowance additional ; provident fund. Bungalow, essential furniture, and servants provided. Applications, with copies of 3 testimonials and the names of 3 other persons for reference purposes, to—Address, No. 724, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Ford Motor Company Limited, Dagenham, Essex. Applications are invited from registered medical practitioners, aged 28–35, for appointment as Junior Assistant Medical Officer. Candidates should have good clinical background and interest in industrial medicine. Salary on appointment £1100 p.a. Subject to medical examination.—Applications, giving full particulars of age, qualifications and experience, and 2 references, should be sent to the Chief Medical Officer, Ford Motor Company Limited, Dagenham, Essex, not later than 3rd October.

Residence, suitable Specialist. Owner retiring. Private practice. Exclusive district.—MILl Hill 1582.

Suitable for Doctor or Dentist. Belgravia. Distinguished corner residence available for immediate occupation. 4 bedrooms, 2 bathrooms, 3 reception-rooms, and study. Side entrance. Lease 35 years. Price £4750.—RICHARD POWELL & PARTNERS, 23, Coleman-street, E.C.2.

Radiographer, M.S.R. 1951, aged 23, desires post in private practice London area. 2½ years practical experience.—Address, No. 727, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Cripplegate Secretarial College, Golden-lane, E.C.1. Tel. : MONarch 2828. For Lady Graduates, and Public, Private, and Secondary Grammar School girls only.—For further information please apply to : The Clerk to the Governors.

Opportunity to acquire complete modern equipment of consulting-room and surgery, bargain to close Estate.—ARTHUR SPEED, Creek-road, East Molesey (Telephone : Molesey 852).

Accommodation available for an ambulatory chronic case in a doctor's house, among beautiful surroundings in a Cathedral city.—Address, No. 726, THE LANCET Office, 7, Adam-street, Adelphi, London. W.C.2.

Rolls Royce and Bentley Servicing. Service and complete overhauls carried out promptly, efficiently, and at minimum cost by Rolls Royce factory trained engineers.—CENTRAL GARAGE (CROYDON) LTD., Fell-road, Croydon (Telephone : CROydon 7464).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE, LTD., 98, Victoria-street, S.W.1 (Phone : VICtoria 0141), who are specialists in this kind of work.

"Pregnancy Diagnosis by the Xenopus Method." 24-hour service.—Spend specimen of urine and £1 1s. fee to : WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (Telephone : MUSeum 5386–7).

X-ray apparatus (diagnostic) wanted, also a portable X-ray apparatus, also a portable operating-table. State condition and price.—Address, No. 722, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

For Sale. "Works of Ambrose Parey," published 1649. Good condition.—Offers to: Address, No. 723, THE LANCET Office, 7. Adam-street, Adelphi, London, W.C.2.

Philips Mobile "D" X-ray Unit for radiography and screening. For operation on any normal A.C. supply from 100 V up to 250 V, 40–60 cycles, single phase. Finish in hospital cream with all bright parts chromium plated. As new. Cost £600. Price, £250 or nearest offer.—Address, No. 725, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Hypnotism. Will all Doctors interested in this subject for Medical purposes please wite to the Secretary, British Society of Medical Hypnotists, 48, Wick Hall, Hove, 2, Sussex.

PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.
Printed by HAZELL, WATSON & VINEY, LTD., London and Aylesbury—Saturday, September 13, 1952.
PRINTED IN GREAT BRITAIN—Entered as Second Class at the New York, U.S.A., Office.

In Essential Hypertension
STOLIC* REDUCES BLOOD PRESSURE

'STOLIC' benefits hypertensive patients in three ways:

1. Mannitol hexanitrate causes marked gradual vasodilation by relaxing the smooth muscle of the arterial system.
2. 'Delvinal' vinbarbital allays apprehension, and tends to reduce fluctuations of blood pressure due to emotional causes.
3. Rutin beneficially influences the incidence of cerebral or retinal hæmorrhage by its effect on capillary fragility.

There are two prescription forms:

'STOLIC' formula:	Mannitol hexanitrate	15 mg.
	Rutin	20 mg.
	'Delvinal' vinbarbital	30 mg.
'STOLIC' Forte formula:	Mannitol hexanitrate	30 mg.
	Rutin	20 mg.
	'Delvinal' vinbarbital	30 mg.

* *'Stolic' is a trade mark*

'STOLIC' and 'STOLIC' FORTE are supplied in bottles of 100 tablets.

SHARP & DOHME

Descriptive literature and sample gladly supplied on request.

SHARP & DOHME LTD., HODDESDON, HERTS.

TB THE CHEMOTHERAPY OF TUBERCULOSIS

'PYCAZIDE'

TRADE MARK BRAND

ISONIAZID

(ISONICOTINIC ACID HYDRAZIDE)

Clinical trials carried out in Great Britain and the United States confirm experimental evidence that this substance has an anti-tubercular activity of a very high order. Further trials, at present in progress, using isoniazid alone or in combination with other anti-tubercular drugs, are designed to investigate the factors governing the development of resistance to the drug. It seems likely that much of the future clinical work with isoniazid will be concerned with combination therapy.

'PYCAZIDE' is supplied as

TABLETS of 50 mg. packed in containers of 100, 500 and 1,000

AMPOULES Sterile solution containing 50 mg. in 2 ml.

SYRUP (Blackcurrant flavoured). The formulation of this syrup has been devised in order to permit greater flexibility of dosage than is possible with 'Pycazide' tablets. One teaspoonful is approximately equivalent to 20 mg. of Isonicotinic Acid Hydrazide.

Full literature from the makers:

HPL HERTS PHARMACEUTICALS LIMITED

WELWYN GARDEN CITY, ENGLAND GM 145